"CLINICAL PROFILE OF LEPTOSPIROSIS WITH SPECIAL MENTION TO ITS MULTIORGAN INVOLVEMENT IN KILPAUK MEDICAL COLLEGE HOSPITAL"

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BONAFIDE CERTIFICATE

This is to certify that **"CLINICAL PROFILE OF LEPTOSPIROSIS WITH SPECIAL REFERENCE TO MULTI ORGAN INVOLVEMENT IN KILPAUK MEDICAL COLLEGE"** is a bonafide work performed by **Dr.IBRAHIM SAMEEM KAN**, post graduate student, Department of Internal Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfillment of regulations of the Tamil Nadu Dr. M.G.R Medical university for the award of M.D. Degree Branch I (General Medicine) during the academic period from July 2013 to April 2016.

Prof. Dr.S.Ushalakshmi M.D.,FMMC.,
Professor and HOD,
Department of Medicine ,
KMC & GRH,
Chennai.

Prof. Dr.S.Ushalakshmi M.D.,FMMC.,
Professor and Unit chief
Department of Medicine,
KILPAUK MEDICAL COLLEGE,
Chennai.

Prof. Dr.R.Narayana Babu M.D.,DCH,
The DEAN
Govt.Kilpauk Medical College
Chennai - 600 010

DECLARATION BY THE GUIDE

This is to certify that the dissertation titled **"CLINICAL PROFILE OF LEPTOSPIROSIS WITH SPECIAL REFERENCE TO MULTI ORGAN INVOLVEMENT IN KILPAUK MEDICAL COLLEGE"** is the Bonafide work done by **Dr. IBRAHIM SAMEEM KAN** during his **M.D (General Medicine)** course in the academic years 2013-2016, at Kilpauk Government Medical College Hospital, Chennai, **under my guidance**.

Prof. Dr.S.Ushalakshmi M.D.,FMMC.,
Professor and Unit chief
Department of Medicine,
KILPAUK MEDICAL COLLEGE,
Chennai.

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LIST OF ABBREVATIONS

ARDS	**:**	Acute respiratory distress syndrome
DIC	**:**	Disseminated intravascular coagulation
WHO	**:**	World health organization
IG	**:**	Immunoglobulins
DNA	**:**	Deoxy ribo nucleic acid
RNA	**:**	Ribo nucleic acid
PT	**:**	Prothrombin time
APTT	**:**	Activated partial thromboplastin time
CT	**:**	Clotting time
LFT	**:**	Liver function tests
ALT	**:**	Alanine amino transferase
AST	**:**	Aspartate amino transferase
L	**:**	Leptospira
CSF	**:**	Cerebro spinal fluid
IL	**:**	Interleukins
GIT	**:**	Gastro intestinal tract
BP	**:**	Blood pressure
IV	**:**	Intravenous
PRP	**:**	Platelet rich plasma

MAT	**:**	Microscopic agglutination test
MSAT	**:**	Microscopic slide agglutination test
ELISA	**:**	Enzyme linked immunosorbent assay
PCR	**:**	Polymerase chain reaction
PBU	**:**	Pan bio units
Hb	**:**	Heamoglobin
TC	**:**	Total count
DC	**:**	Differential count
ESR	**:**	Erythrocytic sedimentation rate

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INTRODUCTION

Leptospirosis has been considered an infrequent zoonoses in India for a long period of time.But for the past two decades there has been a steady increase in incidence of leptospirosis cases in many Indian states particularly Kerala,Gujarat and Tamil Nadu.

With the improvement of diagnostic techniques and clinical expertise there has been a dramatic increase in number of reported cases of this widespread zoonoses.The clinical spectrum of the disease varies from asymptomatic illness to severe and nonreversible renal failure resulting in death.Leptospirosis is diagnosed with the help of specific yet complex laboratory tests as the clinical features of the disease are non specific.Subsequently definite guidelines has been established for the diagnosis of the disease in endemic areas.In India diagnosis of Leptospirosis is simplified using the modified Faine's criteria which makes use of the clinical features as well as the epidemiological and lab data for the effective diagnosis of the disease.

Awareness about the infection is scarce especially in the developing countries as a consequence of which, it is rarely thought of in the differential diagnosis of febrile illnesses.

Among the 824 patients investigated for Acute febrile illness in Kilpauk Medical College hospital for a period of 8 months 67 patients

were diagnosed to have Leptospirosis.Hence this study on the clinical profile of Leptospirosis and its pattern of multiorgan involvement was carried out and the results were analysed.

AIM OF THE STUDY

1) To study and analyse the clinical profile of leptospirosis
2) To study the incidence of multiorgan involvement of leptospirosis

REVIEW OF LITERATURE

BACKGROUND

Leptospirosis is an acute febrile illness common in many parts of the world. Most cases are mild or asymptomatic but the most severe illness, known as weil's disease, may be associated with death through renal failure. Leptospirosis is a worldwide zoonotic infection. It is known by many different local names (e.g. mud swamp, sugarcane fever, fort bragg[3], Japanese autumnal fevers). The major reservoirs are rodents and the organism is passed in their urine for months and can survive in fresh but not brackish water[1]. Man is infected by contact with rodent urine or with meat contaminated by urine.

Awareness about the infection is scarce especially in the developing countries as a consequence of which, it is rarely thought of in the differential diagnosis of febrile illnesses.

Failure to diagnose leptospirosis is particularly unfortunate: severely ill patients often recover completely with prompt treatment but if therapy is delayed or not given, death or renal failure are likely to ensue.

As leptospirosis can be treated by antibiotics especially penicillin group treating physicians should have high clinical suspicion of the disease especially in tropical countries like India and do appropriate investigations to confirm it.

CAUSATIVE ORGANISM

Leptospira species are spirochetes under the taxonomical 0rder Spirochetale and Leptospiracae.This genus consists of pathogenic subspecies namely Leptospirae interrogans and non-pathogenic Leptospirae biflexa. Twenty-three *Leptospira* species with pathogenic (11 species), intermediate (5 species), and nonpathogenic (7 species) status has now been described till date on the basis of phylogeneticity and virulence [(7)].

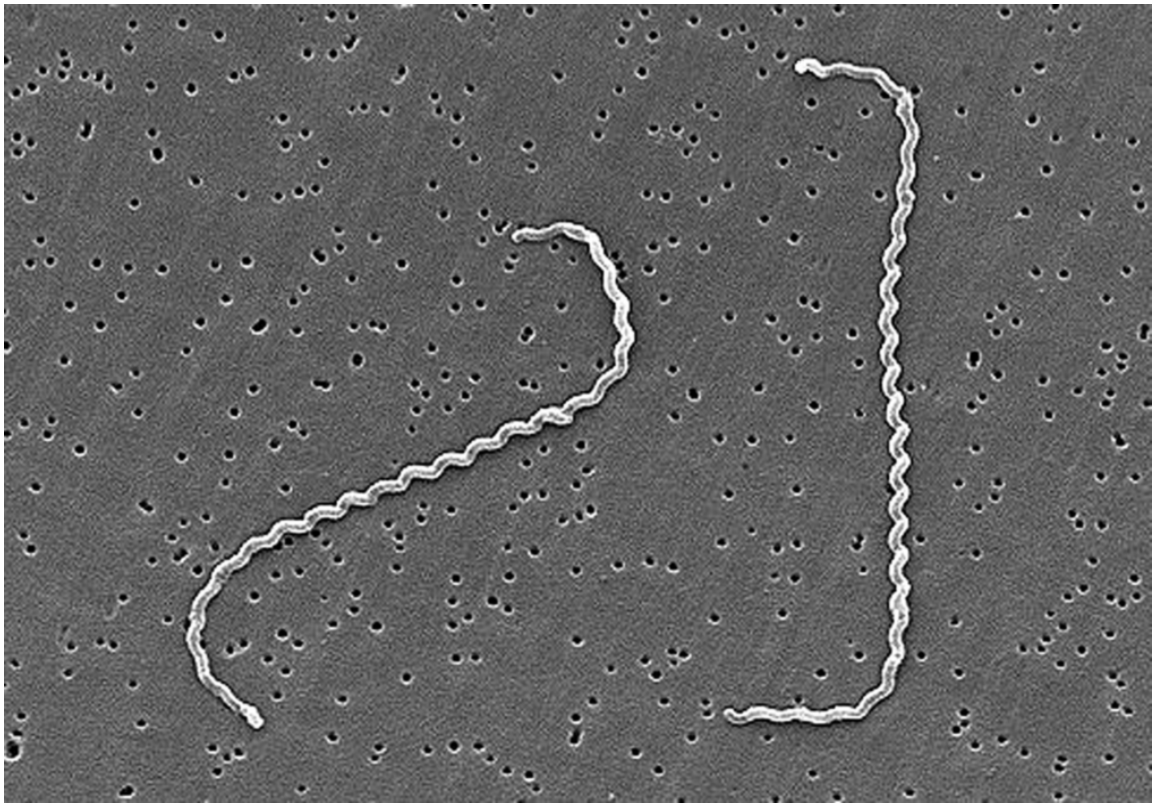
Pathogenic *Leptospira* species are classified into several serovars accordingly.Totally there are over 256 serovars consisting of 26 serotypes.

Leptospira are tightly coiled spirochetes, usually 0.1 μm by 6 to 0.1 by 20 μm, but the occasional cultures may contain longer cells. The helical amplitude is about 0.1 to 0.15 μm, and the wavelength is about 0.5 μm The cells have pointed ends, both of which are usually bent in the form of a distinctive hook .Axial filament (periplasmic flagella) with polar insertions is located in the periplasmic space The structure of its flagellar proteins is complex in nature. Leptospira always exhibit two distinct type of movement, translational and nontranslational Morphologically all are indistinguishable, but the structures of individual isolates differ with subculture in vitro and it can be restored by passage in

hamsters . Leptospires always have a double membrane structure in common with other similar spirochetes, in which cytoplasmic membrane layer and peptidoglycan cell layer are closely interlinked and are overlaid by an outer membraneous structure. Leptospiral LPS has a composition very similar to that of a other gram-negative bacteria , but it has lower endotoxin activity . They are aerobic and travel with a corkscrew like motion. The unstained organisms can be seen by dark-field or phase contrast microscopy. Silver staining is the method of choice for demonstrating leptospira in the tissue specimens.They may be also stained with carbol fuschin counterstain [7].

Leptospira are obligate aerobic organisms with optimum growth temperature of around 28 to 31°C. They produce both catalase as well as oxidase.. They thrive and grow in simple medium enriched with vitamins (vitamins B_2 and B_{12} are the growth factors), long &medium chain fatty acids, and ammonium salts .The long chain fatty acid is utilized by leptospira as the sole source of carbon and are metabolized by β-oxidation.

LEPTOSPIRA THROUGH SCANNING MICROSCOPE



EPIDEMIOLOGY

Current information on global human leptospirosis varies but indicates that approximately 1 million severe cases occur per year, with a mean case–fatality rate of nearly 10%[(15)]. As a zoonoses, leptospirosis affects almost all mammalian species and represents a significant burden. Rodents, especially rats, are the most important reservoir, although other wild mammals as well as domestic and farm animals may also harbour these microorganisms.These spirochetes can establish themselves inside the urinary pathway of the affected individual for many days. Some serovars appear to be preferentially adapted to

select mammalian hosts. For example, *L.□interrogans* serovar Ictero haemorrhagiae is primarily associated with the Norway rat, *L.□interrogans* serovar Canicola with canines, and *L.□interrogans* serovar Pomona with swine and cattle[5].

The vast majority of infections with *Leptospira* cause no or only mild disease in humans. A small percentage of infections (~1%) lead to severe, potentially fatal complications. The total number of reported illness due to leptospira is rarely known because of the highly nonspecific nature of the illness. Risk factors include direct or indirect contact with animals, including exposure to water and soil contaminated with animal urine. The increasing rodent population is directly proportional to the incidence of the disease.

Swimmers and other athletes involved in watersports are at increased probability of contracting the disease due to the natural habitat of the organism. Large proportions of patients acquire the infection while traveling in tropical countries, usually during adventurous activities such as whitewater rafting, jungle trekking, and caving. Furthermore recent data indicates that leptospirosis can also be contracted as a result of untoward lab errors or via accidental exposure to infected water source more frequently than has generally been thought and can also result from an animal bite.

In a retrospective study of 9335 cases by Paulo H Yesuda et..al ,Adolf Lutz institute,Brazil between 1969 and 1997,the disease was found endemic throughout Brazil.Middle aged persons ranging from 20-39 years of age were the most frequently affected (32.40%).Males were the most frequently affected (87%) with an overall ratio of male to females of 6.7:1.The mean incidence annually was 0.53 cases per 1 lakh .The cases occurred in clusters mainly in January to April every year with peaks observed in 1991 and 1996 during which there was heavy rainfall.

Leptospires nest in the renal tubules of mammalian hosts and are shed in the urine. They can survive for several months in the environment under moist conditions, particularly in the presence of warmth (above 22°C) and a neutral pH (pH□6.2 to 8.0).

These conditions occur all year round in the tropics but only during the summer and autumn months in temperate climates. Roughly 160 animal species harbour organisms, but rodents are the most important reservoir. Carrier rates of over 50% have been measured in Norway rats, which shed massive numbers of organisms for life without showing clinical illness.[(1)]

The incidence is significantly higher in warm-climate countries than in temperate regions ; this is due mainly to longer survival of leptospires in the environment in warm, humid conditions. However,

most tropical countries are also developing countries, and there are greater opportunities for exposure of the human population to infected animals, whether livestock, domestic pets, or wild or feral animals. The disease is seasonal, with peak incidence occurring in summer or fall in temperate regions, where temperature is the limiting factor in survival of leptospires, and during rainy seasons in warm-climate regions, where rapid dessication would otherwise prevent survival.

The reported incidence of leptospirosis reflects the availability of laboratory diagnosis and the clinical index of suspicion as much as the incidence of the disease.

Table 1: Distribution of Leptospira serovars in India

State	Animal species	Serovars
High prevalence		
Tamil Nadu, Kerala, Andaman	cattle, buffalo, sheep, goats, pig	pyrogenes, pomona, australis, utumnalis, hebdomadis, hardjo, icterohaemorhagiae
Moderate Prevalence		
Maharastra, U.P., M.P., Gujarat, Karnataka	cattle, buffalo, goats, sheep, pigs, dogs, horse	pomona, hardjo, canicola, javanica, icterohaemorhagiae, pyrogenes,
Rarely Reported		
Punjab, J&K, Rajasthan, North-Eastern Hills, Himachal Pradesh	cattle, sheep	icterohaemorhagiae, pyrogenes, canicola

*Based on isolation and serology (Source - WHO, 2006)

PATHOGENESIS

The abraded mucosa is the ingoing pathway for the organism.following this a widespread . Leptospires are disseminated through blood and can be recovered from almost all organs within a time span of roughly 48 hours of entering the host.

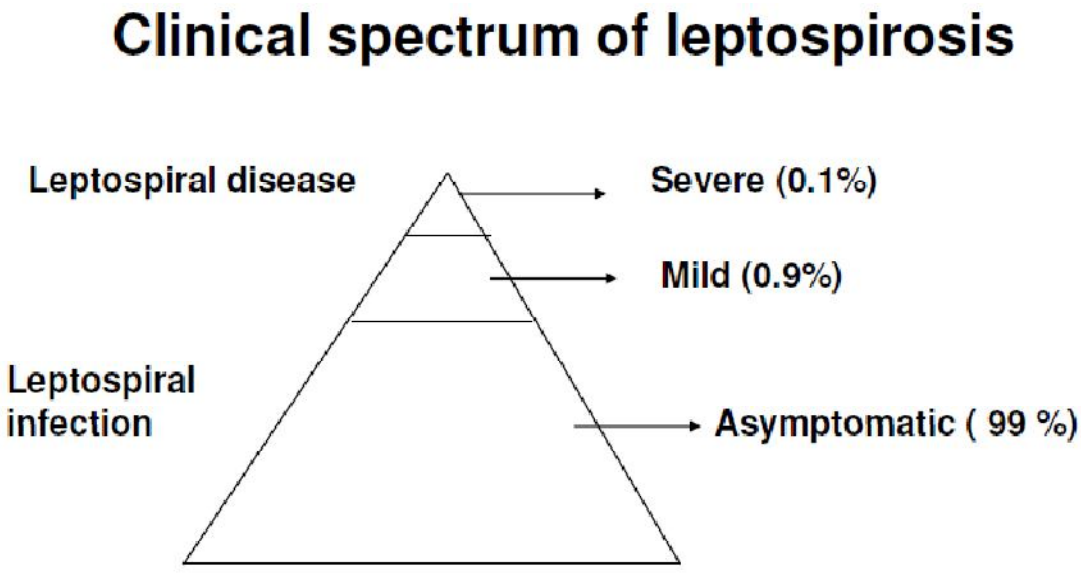
Leptospiraemia lasts for about 4 to 7 days and ends when the specific antibodies appear in blood stream. The bacteria can persist for months in the renal and ocular tissues.Bacteremia ensues during the acute, leptospiremic phase of the disease progress[(2)].

Three mechanisms are involved in the pathogenesis of tissue injury in leptospirosis:

1. Direct effect of leptospires.

2. Immunological reaction.

3. Non- specific factors



The host responds to bacteremia by producing agglutinating antibodies which in combination with complement factors, are leptospiricidal. The bacteria is swiftly eliminated from the host organs except the brain and kidneys. Leptospires that survive in brain multiply slowly.But, in kidneys they multiply rapidly in tubules and are shed in the urine.Thus the leptospires may persist in the host for days to

months,whereas in rodents they can be shed in their urine for lifetime of the animal. This leptospiruric urine forms the main vehicle of transmission.

The exact mechanism through which leptospira causes the disease remains unclear, as neither endotoxin or exotoxin has been associated with their replication. The Damage to endothelial layer of the capillaries and resultant interference with the blood flow is responsible for the effects associated with leptospirosis. The most pathagnomic feature of severe leptospirosis is progressive impairment of liver and renal function. Renal failure is the most common cause of death in leptospirosis. The inherent lack of considerable cell destruction in the disease is reflected by complete recovery of hepatic and renal function in survivors.

The host's defence immunologic response to the spirochete is responsible for lesions that occur in the late phase of this disease; this phenomenon explains the ineffectiveness of antibiotic drugs once the symptoms of disease has been present for duration of 4 or more days.

Some critically ill subjects typically have marked leucocytosis in peripheral smear but rarely any leucocytic infiltrates in target organs, a pattern which is produced by some endotoxins. Fatally infected animal models and certain human patients had clinical picture to those classically produced by endotoxins of Gram-negative bacteria. An endotoxin like

material is present in cell wall of leptospira but they lack the ketodeoxyoctanoate component of a true endotoxin.

TARGET ORGANS

KIDNEYS

Renal failure constitutes the major cause of mortality in leptospirosis. In kidneys, leptospires invade the interstitium, tubules, as well as the tubular lumen, resulting in classical interstitial nephritis like pattern and necrosis of the tubules.Inflammation of the capillary membranes is also found frequently.Impaired kidney perfusion is identified as the fundamental pathophysiology.The oliguria is readily reversed by administering intravenous fluids in all patients, hence indicating that volume depletion is common. The reason for hypovolemia is usually multifactorial .Renal magnesium wasting has been demonstrated more recently but its clinical significance is not known. There is also a extensive endothelial damage that results in shift of fluid from the intravascular to the extracellular compartment. [(1)]

LIVER

There is extensive centrilobular necrosis as well as proliferation of the kupferr cells in the parenchyma. Increased serum bilirubin may be

due to toxic intermediate metabolites. Associated cholestasis may also be present.

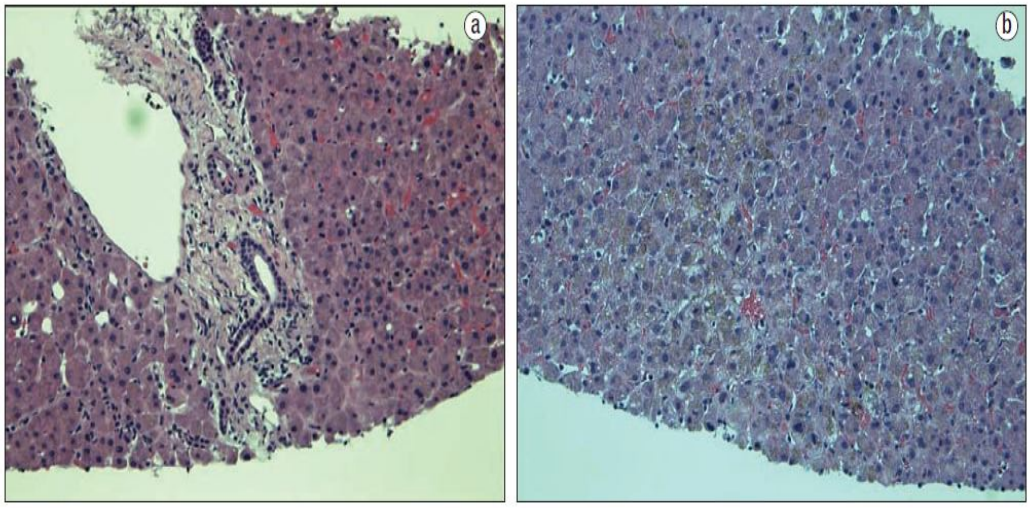


Figure 1. Liver biopsy results showing (a) mild periportal hepatitis with hepatocanalicular cholestasis and (b) an increase in mitotic activity, which suggests regenerative changes from an injury.

MUSCLE

There is early myalgia due to colonisation of skeletal muscle fibres by leptospires. Muscle biopsy demonstrates extensive vacuolation of myocyte cytoplasm with fragmentation.Spirochetal antigens are demonstrable by immune fluorescence inside the muscle fibres.Once the antibodies begin to outpour the myalgia resolves.

LUNGS

Lung involvement is a result of interstitial and alveolar damage ending in extensive hemorrhage. Lung autopsy results include extensive intraalveolar hemorrhage along with resultant alveolar damage.

Leptospires can be demonstrated in pulmonary specimens, but few intact spirochetes present at autopsy suggests a immune mediated reaction involved.leptospirosis pulmonary hemmorrhage syndrome is now found to be closely linked with linear immunoglobulin deposition with fixation of complement on the alveolar membrane[2]

HEART

The heart is affected in the form of hemorrhagic myocarditis with other factors like hypovolumia,dyselectrolytemia contributing to cardiac dysfunction.Subtle ecg changes like AV blocks as well as serious ventricular arrthymias can occur in the course of the disease

EYES

The vitreous and Aqeous humour act as a protective medium in which the leptospires proliferate during the leptospiremic phase .The main presentation being anterior uveitis which is attributed to the presence of leptospires in the anterior chamber.

VASCULAR SYSTEM

Capillary leakage can result in persistent hypovolumia and shock.In due course the patient may develop Disseminated Intravascular Coagulation as well as Thrombotic Thrombocytopenic purpura.Low platelets is usually associated with bad prognosis.

CLINICAL FEATURES

Subclinical disease is extremely common and less than ten percent of illness end in severe icteric disease. Even virulent serovars like *L.interrogans* Icterohaemorrhagiae often end in anicteric than icteric presentation.. The usual incubation time is 9 days, with a range of 3 to 26 days. The duration of the incubation time has nothing to do with the disease course. Once signs and symptoms of the illness develop it follows a biphasic course.with an initial fever phase , there is defervescence of fever with symptoms improving only to follow by a second phase of illness. The diagnostic value of this biphasic presentation has been overemphasized.

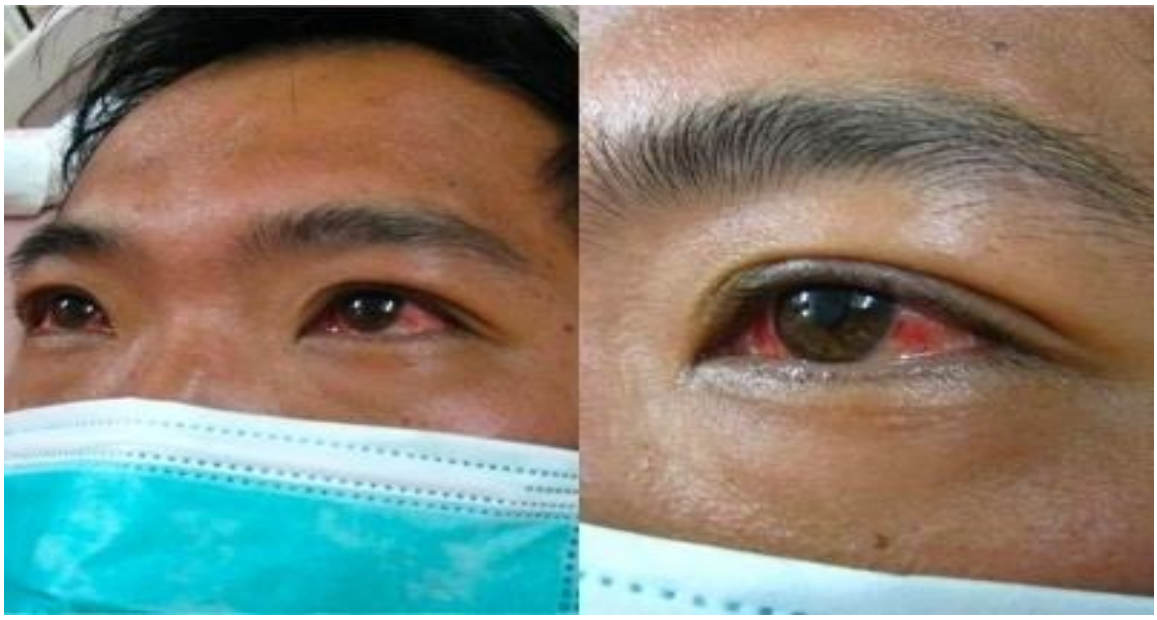
ANICTERIC LEPTOSPIROSIS

Symptoms and signs

Usually, the disease starts with acute onset of intense headache, fever, chills, and body pain. Pyrexia commonly exceeds 40°□C (103°□F) and is mostly preceded by rigors. Myalgia can be very excruciating and affects most commonly the thigh, calf and lumbosacral region.Conjunctival suffusion is a characteristic clue which appears 3 days after fever and involves the bulbar conjunctiva mainly .There is no Pus and serous secretions or matting of eyelashes.Early suffusion may be

overlooked sometimes. Less common signs include pharyngeal irritation,hepatosplenomegaly,generalised lymphadenopathy, and skin lesions[3].

Characteristic conjuctival suffusion in leptospirosis.



ICTERIC LEPTOSPIROSIS (Weil's disease)

Symptoms and signs

This life-threatening disease is characterized by a triad of jaundice, renal dysfunction, hemorrhagic manifestations with a very high mortality.Jaundice marks the hallmark of severe leptospirosis, yet mortality do not occur because of hepatic failure. The degree of jaundice do not reflect on mortality.Jaundice first occurs between the fourth and ninth days of fever, reaching a peak 4 or 5 days later, and can continue

for an average of 30 days[2]. Hepatomegaly is usually demonstrable in the majority of patients and there is no residual liver dysfunction.

Bleeding tendency occurs in anicteric cases but usually more prevalent in severe disease. Purpura,epistaxis,bleeding gums, and haemoptysis are the most common presenting haemorrhagic manifestations, but mortality can occur from subarachnoid bleed and exsanguination from GI bleeding.Subconjunctival haemorrhage being an extremely useful clinical feature when combined with icterus and suffusion, produces opthalmic features strongly supportive of leptospirosis

Renal failure is a life threatening complication of Weils disease, although all forms of the disease may be linked with mild renal dysfunction.Oliguria invariably begins in the 2nd week of fever, but can appear earlier. Complete anuria indicates worst prognosis very common in patients presenting late with frank uraemia and irreversible damage[7].Since renal failure onset is very rapid in leptospirosis, symptoms of uraemia are seldom encountered. Vomiting, mental disturbance with confusion are encountered early and they progress swiftly to convulsions and coma in very severe patients.Impairment of sensorium in a person with severe leptospirosis is usually as a result of uraemic encephalopathy, whereas in anicteric cases aseptic encephalitis

is the casual factor. Renal parameters revert back to normal in survivors of the disease, but sometimes minor detectable abnormalities may persist for few months [14].

"Leptospirosis-associated severe pulmonary haemorrhage syndrome (SPHS) is recent widespread problem with a case fatality rate almost reaching 50%. This dreadful complication of the disease can occur with or without jaundice and kidney failure. Blood stained sputum is the cardinal sign, but can occur late. Real-time PCR has shown the critical threshold for morbid outcomes such as SPHS and death is a leptospiral count of 10,000 or more bacteria/ml of blood."

The first ever report of leptospiral pneumonia in India was from north Andaman. In this study where serum samples were collected from suspected patients during October-November 1993, 66.7% of the patients showed significant titres of antibodies against leptospira24. In a clinico-epidemiological study of hospitalized 22 cases of severe leptospirosis done by Singh.S.S, et.al., the disease had represented as two separate clinical syndromes, the hepato-renal form and the pulmonary form.

Even though the hepato-renal complication had occurred late in the course of the disease the pulmonary complication occurred early and the case fatality rate in those patients were high (6.7% vs 42.9%). Even

though pulmonary tuberculosis is the most common cause of tropical lung infection, leptospirosis as a cause of tropical lung infection has also been reported. Even though severe pulmonary complications in leptospirosis are rare, complications like adult respiratory distress syndrome (ARDS) has been a well recognized severe form of acute respiratory failure.

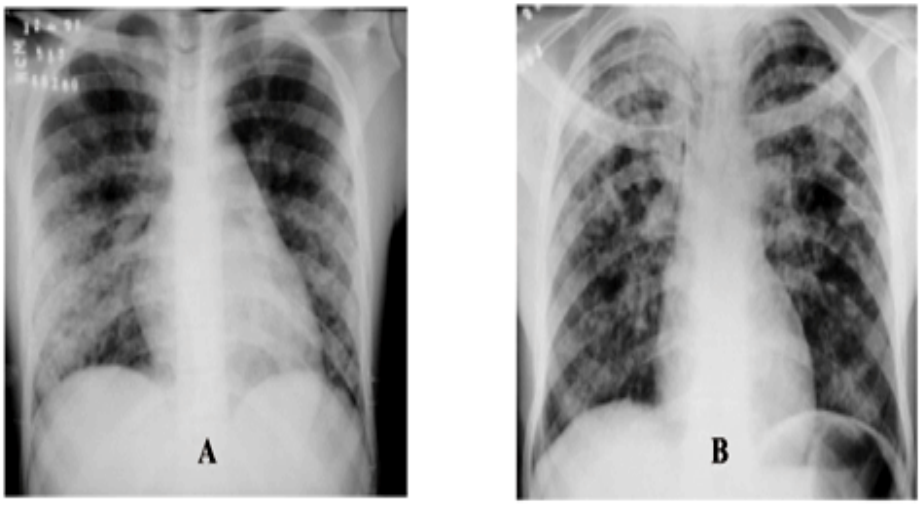
In a prospective study by Kiatboonsri S, et al.,where 46 cases of ARDS were studied. In this study it was found that leptospirosis was also a potential factor in the causation of ARDS27. Leptospira as a causation of pneumonia is extremely rare but cases of atypical pneumonia in leptospirosis has also been described. Another characteristic lung manifestation of leptospirosis that has been described is the Andaman hemorrhagic fever. Clinically the disease has been occurring as fever (101-103°f) of 2 to 3 days duration,cough with sputum, often tinged with blood and generalized body aches.

"Aseptic meningitis /meningoencephalitis may be seen in leptospirosis. In the meningitic form of the disease, the patient may have some of the other manifestations of Weil's syndrome like myalgia, subconjunctival hemorrhage, jaundice and renal failure along with clinical features of meningitis associated with increased CSF protein and lymphocytes. Leptospirosis has also been reported to produce cerebral arteritis and polyradiculitis.

Patients with leptospirosis may present predominantly with meningitis and the CSF contains moderate number of lymphocytes and mildly elevated protein without altered glucose. Cerebral arteritis is an unusual late complication-Mayomaya syndrome is caused by obstruction of the internal carotid arteries near the circle of willis."

ARDS PATTERN IN LEPTOSPIROSIS

Figure 1. Chest radiograph of two patients with leptospirosis showing the pattern of bilateral alveolar infiltrate. A – Areas of confluent consolidation located in peripheral zones of the inferior lobes. B – Diffuse nodular and small, patchy opacities



A total 23 patients were diagnosed positive for leptospirosis from July to December 2010 were analysed by Virendra C Patel et...al.Among the infected patients fever was the universal presenting feature.16 patients (69.56%) had mild fever whereas 7patients (30.43%) presented with high fever.Clinical jaundice was present in 16(69.56%) subjects.11 individuals (47%) had conjuctival suffusionHeadache (12 Patients-51%) and meningsm 4(17%) were the other notable clinical presenting

features.Myalgia was also very common being present in 16 (69%) of the subjects.

In another clinical study by Karoke M.N. et..al in kerala during the period of 1988 to 94,among 976 confirmed leptospirosis cases,the most common presenting clinical feature was the common leptospiral syndrome compromising of fever,bodyache and muscle pain.the other common presenting complaints were meningism,loose stools and vomiting.

LABORATORY FINDINGS

Hyperbilirubinaemia is a result of increase in both conjugated (direct) as well as unconjugated (indirect) bilirubin, but elevations of the direct fraction occurs often. Prothrombin time that is prolonged can be easily corrected by the administration of vitamin K.

Modest elevation of levels of serum alkaline phosphatase are typical as a result of mild hepatocellular necrosis; more than fivefold increase in aminotransferase levels occur rarely.

In jaundiced patients leucocytosis ranging from 15 to 30 × 10^9/litre, and neutrophilia is a constant finding. Anemia is also very common and multifactorial; blood loss and uremia is the major contributor, and intravascular haemolysis less often.Thrombocytopenia occurs, but

decrease in platelet count is insufficient to be associated with active bleeding.The urinary specific gravity is high. Hypokalaemia and hypomagnesemia as a result of renal wasting can occur.

URINE ANALYSIS

The colour of urine varies with the degree of serum bilurubin.The urine output may be normal or reduced.Proteinuria as well as bilurubinuria can be present.In severe patients urine may show bile excretion.centrifuged urine deposit may reveal the bile excretion.

TOTAL COUNTS

There is predominant leucocytosis ranging from 15,000 to 30,000cells/mm3.Since the capillary membrane damage is the main reason for the bleeding manifestations the coagulation profile may remain normal during the disease course.ESR values are high and there is anemia mainly secondary to blood loss.

LFT

As said there is mainly increase in the levels of conjugated bilirubin.Liver transaminases may show moderate elevation and alkaline phosphatase is also uniformly elevated in almost half of the affected individuals.

RFT.

There is marked increase in the levels of both urea as well as creatinine and deaths due to leptospirosis correlates with blood urea levels.Upto 40% of the presenting cases may end up in non oliguric renal failure and hence contributing the delayed diagnosis of renal dysfunction.

CSF ANALYSIS

CSF may show elevated protein fraction whereas the sugar levels are normal.Peculiarly the levels of CPK-MM (creatinine phosphokinase) is elevated in nearly 50% of the patients.The other remaining fraction may show normal CSF studies with only mild increase in protein alone.

DIFFERNTIAL DIAGNOSIS

It is vital to consider leptospirosis infection as a differential diagnosis for lung hemorrhage or sudden respiratory failure.Particularly in patients who are exposed to highly endemic areas.

Leptospirosis being a multisystem disorder can be mistaken to be a simple viral fever,typhoid or influenzal prodrome.Similarly Weils disease is usually confused with the other causes of fever with jaundice which may include

1.Malaria

2.Overt septicemia with high bilirubin

3.Acute viral hepatitis

4.Viral prodromes

The main differentiating feature of leptospirosis is acute onset headache with myalgia and conjuctival suffusion in comparison with the gradual onset of symptoms of mayalgia.Conjuctival findings are characteristically absent in fevers including malaria and typhoid.

DIAGNOSIS OF LEPTOSPIROSIS

The following are the main factors involved in diagnosing the disease

1. To confirm the diagnosis of leptospirosis

2.to analyse the causative serovar, the probable source of infection, identify the reservoir and its source

During the initial bacterimic period (< 1 week) leptospires can be readily isolated by culture and polymerase chain reaction.

Culture:

Most confirmatory diagnosis is separating spirochetes by culturing infected substances which include blood as well as urine. In early phase blood or cerebrospinal fluid is the preferred substrate for culture whereas during the later stages urine is preferred.

Blood culture is valuable because it is of vital importance in identifying the causative serotype.it also plays a major role in assessing the sensitivity of antibiotics and the development of new vaccines.

The media that are used in culture are:

1) Korthof”s medium

2) Stuart’s medium

3) EMJH medium (Elling hausens and McCullough's, Johnson and Harris)

4) Fletcher's semisolid medium

Fletcher's semisolid medium and Stuart's medium are the culture media generally recommended. The growth of the organism in culture takes a long time and may not be relevant from the treatment point of view. The primary culture is incubated at the optimum temperature and samples from culture are examined by dark field microscopy every 3 days. It may take upto 4 weeks for the organism to grow.

The generation time of leptospirosis is 7 to 16 hours; the rate of multiplication is increased by shaking or stirring liquid cultures. Growth is usually detected after 6 to 14 days. In liquid medium the growth is faintly turbid and when the tube is shaken gently it has the appearance of "shot silk". In semisolid media, the upper part becomes turbid as the leptospires multiply, one or more characteristic flat discs develop several mm to 3 cm below the surface (Dinger rings)[5]

PCR

PCR method has both higher sensitivity as well as specificity, but the problems are technical difficulty and cost.

Animal inoculation.

Lab animals can be used for isolating leptospira from contaminated specimens and also in maintaining the recent isolates. They are also helpful in recovering single serotypes from cultures.Infant animal,is usually preferred reason being older animal resisting infections.

The animal population must also be free from endemic leptospirosis; guineas young rabbits hamsters, gerbils, ,white mice,deer mice and young chicks are potential animals for culture.The infected material is injected intraperitoneally into the abdominal cavity. Subsequently the peritoneal fluid washings can be observed in dark field microscopy for active leptospira.

Serovar specific tests:

Microscopic agglutination test (MAT): “MAT is considered as the gold standard diagnostic test because of its higher specificity”.Following are the practical difficulties in using MAT

a. The antibody levels start rising and they begin to peak in second or third week only, thus reducing its sensitivity.

b. The most conclusive criteria is the 4 fold rise in titre of leptospirosis which makes the availability of another sample mandatory,thus posing a practical difficulty.

But in such conditions,one single high antibody titer is sufficiently considered as diagnostic criteria. Also MAT titers may persist upto 10 yrs which would eventually alter the current scenario which makes the use of alternate criteria

Therefore a single titre of 1:100 is usually taken to be significant but the sensitivity depends entirely on prevalence.Among high prevalence sites single titre of 1:100 or 1:200 is usually considered as low whereas titres of > 1:400 is diagnostic.In non endemic areas 1:100 is suffient enough to make the diagnosis.

Its always preferable to couple high titre results with the rapid tests.Negative rapid tests usually suggest past episode of infection.Particularly in places like Andaman islands a titre of 1:200 is taken to be diagnostic.

Genus specific tests

The commonly employed genus specific tests include ELISA,Macroscopic slide agglutination test (MSAT), latex agglutination test, Dipstick tests (mainly Leptodipstick, LeptoTek lateral flow test) and Lepto TekDry Dot test.Invariably the genus specific tests are the

mainstay choice for the diagnosis of current infections.The main advantage is that these tests are relatively simple to perform yet more sensitive and becomes positive much earlier than Microscopic agglutinations tests. These diagnostic tests easily detect genus specific antibodies,being shared by both pathogenic as well as saprophytic leptospires.

Rapid tests may become positive as early as 4 to 6 days because they detect specific IgM group of antibodies and hence help in early diagnosis of cuurent leptospiral infection.

Criteria for Diagnosis of Current Leptospiral infection

Confirmed dianosis

1. Culture: Positive

2. MAT: presence of Seroconversion or atleast 4 fold rise in the titre

Probable diagnosis

1. Rapid tests- Positive

2. MAT- High titers in a single sample

Comments

The rapid tests are usually adequate for the diagnosis of current leptospiral infection which can be done easily even in smallscale labs of

both rural as well as urban areas..If rapid tests turns out to be positive, the next step is confirming the diagnosis with MAT.

MANAGEMENT

The response to treatment and reduction in morbidity and mortality of leptospirosis infection primarily depends on the early diagnosis and initiation of appropriate treatment.

The mainstay management of leptospirosis is antibiotic therapy coupled with symptomatic treatment of fever,myalgia and dearranged renal and liver parameters.Correction of fluid and electrolyte imbalance is ideal.

Placebo-control studies in various endemic regions have proved the efficacy of Doxycycline in early leptospirosis, and intravenous penicillin effectiveness in adults with severe disease.. Antibiotics are the mainstay treatment of all patients with leptospiral disease regardless of age or duration of the disease.. Doxycycline is given at a dose of 100 mg per oral two times a day for 7 days. Patients who donot tolerate oral drugs or patients seriously ill are treated parenterally.Intravenous penicillin G is the preferred drug of choice in proven cases and its administered in the dose of 1.5 million units every 6^{th} hourly for atleast 1 week. Recent trials from Philippines show that treatment with ceftriaxone, cefotaxime, and doxycycline had almost equivalent efficacy similar to intravenouus

penicillin.In mild to moderately severe lepospirosis it is proven that Doxycycline as well as azithromycin has equal efficacy in presumptive treatment of leptospirosis, scrub typhus, or dual infections.In case of penicillin hypersensitivity Erthyromycin can be tried.Resistance to the above mentioned drugs has not been yet encountered but there are cases of treatment failure.During the initiation of antibiotic therapy there may be a Jarish-herxheimer reaction (increase in the clinical severity of symptoms with the initiation of treatment).Such reactions are no contraindication to discontinue the antibiotics.

Renal failure is the most common cause of death in patients affected by leptospirosis.It should be counteracted by peritoneal dialysis or Haemodialysis if needed and other supportive measures[20].

PROGNOSIS:

Most patients recover. Overall mortality used to be about 15 – 40% and has been reduced to about 5% with better management. Death is usually due to renal failure but it can also occur due to massive bleeding or cardiac and pulmonary complications.

PREVENTION

Doxycycline, when taken 200 mg once a week, prevents infection by *L.interrogans*.Widespread Doxycycline chemoprophylaxis is not

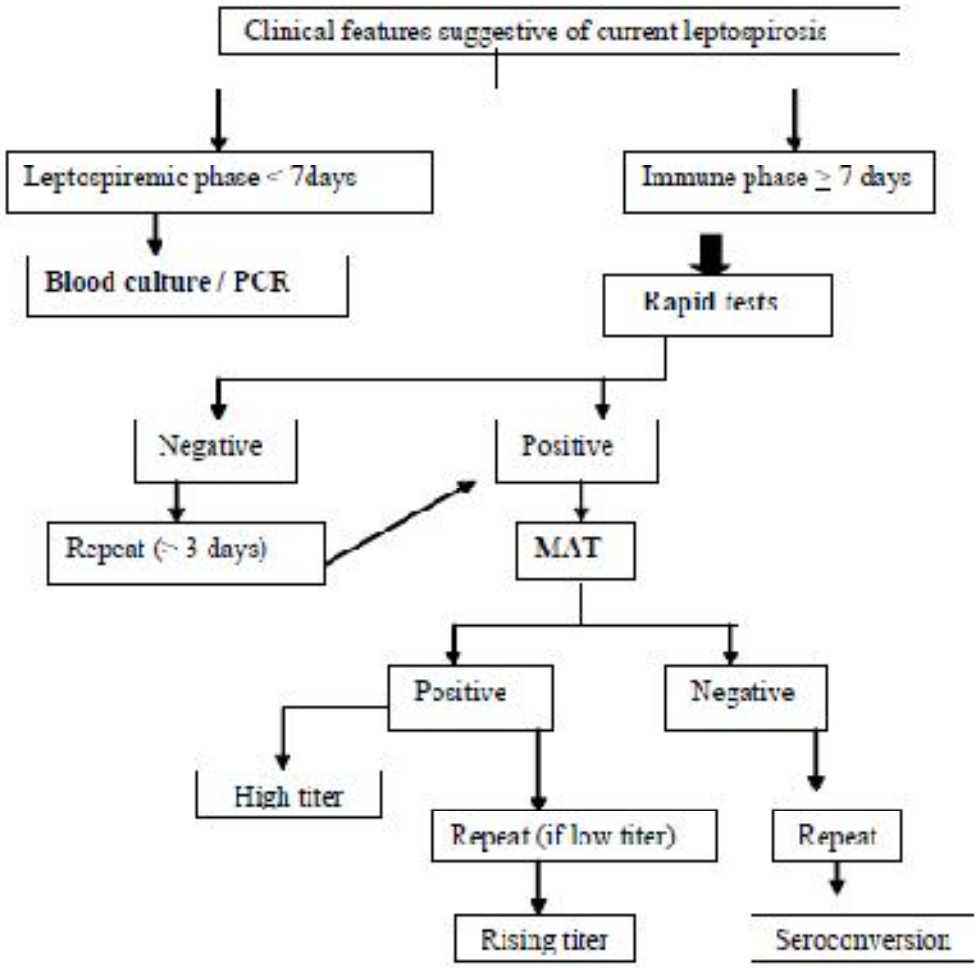
usually indicated, but persons exposed to high endemic areas like military personal or certain farmers can make use of Doxy prophylaxis [15].

Preventing exposure to the disease is not always possible since leptospirosis is a widespread zoonoses.The primary preventive measure is to identify the possible source and eliminating the organism from the environment.The best possible way to prevent leptospirosis is to avoid contact with animals and areas exposed to their contaminated urine.The main group of people at risk of contracting the disease are rice,sugarcane farmers,sewer workers, adventure travellers,watersport enthusiasists and military personnel.

Immunization of animals with vaccine can prevent leptospirosis in animals and reduce transmission of leptospira infection to other animals and humans40. Although immunization of humans was purportedly successful in prevention of leptospirosis among mine workers of Japan and Poland and rice farmers in Italy and Spain, more recent human vaccine development and use has been hampered by limited number of serovar antigen they have contained and the serovar specific immune response they elicit.

All personnel indulging in high-risk activities mentioned above should make use of protective coverings and they need to stick to a high standard of hygiene.Eye goggles,face protecting masks,rubber boots should be used in all possible situations to decrease the risk of transmission.

APPROACH TO DIAGNOSIS OF LEPTOSPIROSIS [22]



MODIFIED FAINES CRITERIA [26]

TABLE 2 | Modified Faine's criteria (2004)

Clinical data (Part A)		Epidemiological factors (Part B)		Bacteriological and laboratory findings (Part C)	
Headache	2	Rainfall	5	*Isolation of leptospira in culture—Diagnosis certain*	
Fever	2	Contact with contaminated environment	4	**Positive serology**	
Temperature >39°C	2				
Conjunctival suffusion	4	Animal contact	1	Elisa IgM positive*	15
Meningism	4	Total	10	SAT—Positive*	15
Muscle pain	4			MAT—Single high titer*	15
Conjunctival suffusion + Meningism + Muscle pain	10			MAT—Rising titer/ seroconversion (paired sera)	25
Jaundice	1			Total	
Albuminuria/Nitrogen retention	2			* **Any one of the tests only should be scored**	
Total score					

Presumptive diagnosis of leptospirosis is made of:

Part A or Part A and Part B score : 26 or more

Parts A, B, C (Total) : 25 or more

A score between 20 and 25 suggests leptospirosis as a possible diagnosis.

Abbreviations: MAT, Microscopic agglutination test; SAT, Slide agglutination test

METHODOLOGY

MATERIALS AND METHODS

OBJECTIVES:

1) To study and analyse clinical profile of Leptospirosis.

2) Laboratory findings of Leptospirosis.

3) To study the incidence of Multi organ involvement of Leptospirosis.

STUDY DESIGN:

Cross sectional study (descriptive)

STUDY POPULATION:

A total of 67 patients who were admitted with fever at Kilpauk Medical College Hospital, Department of Medicine, over a period of 8 months who have been diagnosed to have leptospirosis fulfilling the inclusion and exclusion criteria.

JUSTIFICATION:

In spite of major successes against infectious diseases in 20th century, new infections have emerged and old ones re-emerged in recent decades. Leptospirosis appears to be on the increase in Karnataka, Kerala, Tamilnadu and Andaman during last two decades probably due to

increased farming and inadequate rodent control. Since there is a steady increase in cases of leptospirosis to Kilpauk hospital since last 4-5 years, the aim of the study is to study clinical profile of leptospirosis with special reference to multi organ involvement. A total of 67 cases proved to be having leptospirosis were to be admitted and analysed

PLACE OF STUDY: Kilpauk Medical College Hospital, Chennai.

SAMPLE SIZE: 67 (As per formula)

Applying the sample size formula :

N=Z^2{P*Q}/ l^2

- Z; with 95% confidence interval
- P: prevalence ofsubclinical hypothyroidism
- Q: 100-p
- L: relative precision is 50%

So on applying this formula my sample size was around 67.

DURATION OF STUDY: 8 MONTHS

METHOD OF COLLECTION OF DATA:

Data for the proposed study was collected in a pre tested proforma which includes various socioeconomic parameters like age, sex, occupation etc. Clinical, Biochemical and hematological profile of these patients were obtained from the date of admission, during the hospital

stay. The analysis of the data was made on the basis of important statistical parameters like the Mean, Standard deviation, Standard error, T-test and proportion test where applicable. All values are compared at 5% or 0.05 and 1% or 0.01 levels of significance for the corresponding degree of freedom to arrive at conclusion regarding the objectives of the study.

METHODS :

Patients satisfying the inclusion & exclusion criteria are enrolled into the study.

INCLUSION CRITERIA:

Patients admitted to the medical wards of Government Kilpauk Medical College Hospital with fever due to infectious disease of duration of more than 5 days who were tested positive for leptospirosis utilizing MSAT test (Macroscopic Slide Agglutination Test) (titers > 2+) and satisfying Modified Faine's criteria were taken up for the study. These patients were evaluated for relevant epidemiological, clinical and lab profiles.

EXCLUSION CRITERIA:

1) All known patients with leptospirosis, who were also positive for acute febrile illness like malaria, typhoid, dengue, brucella, viral hepatitis, ricketssiae.

2) Patients having past history of systemic illness involving liver, kidney CNS .

THE FOLLOWING INVESTIGATIONS ARE DONE TO ASSESS THE STUDY:

1) Complete blood picture

2) Routine urine analysis

3) Random blood sugar

4) Blood urea

5) Serum creatinine

6) Chest x-ray pa view

7) HIV- antibodies detected by ELISA

8) IGM antibodies to leptospira

9) QBC for MP

10) LFT

11) Platelet count

12)Ultrasound abdomen

13) Widal test

14) IGM antibodies to dengue

15) CSF analysis(if necessary)

16)Kidney biopsy(if necessary)

ETHICAL ISSUES:

Patients/relatives will be explained about the study.

Patients will be included in the study after obtaining written informed consent.

SAFETY:

- No harm done to the patient
- No extra expenses for the patient
- Informed consent was obtained

ETHICAL CLEARANCE:

All necessary ethical clearance was obtained from the ethical committee, Kilpauk Medical College &Hospital, Chennai.

LIMITATIONS OF THE STUDY

Sample size was achieved with less absolute precision, hence the results of the study will have wide variability. Due to limited resources and practical constraints this study is being carried out with a small sample size. Thus the appropriate representation of the population and better outcomes could be attained by increasing the sample size

STATISTICAL ANALYSIS:

Statistical analysis was done by SPSS software.

Chi square test and p value was used for statistical analysis.

p value less than 0.05 was considered significant.

RESULTS AND ANALYSIS

Results

In the present study, 67 confirmed cases of Leptospirosis were admitted to the Department of Medicine in Government Kilpauk, Medical college, Chennai from January 1st 2015 to August 31st 2015. The total number of acute febrile illness cases admitted during the study period were 824, out of which Leptospirosis constituted 8.1%.

Table no 1: Prevalence of Leptospirosis among acute febrile illness

Total number of cases of acute febrile illness	824
Total number of confirmed cases of Leptospirosis	67

Graph no 1: Prevalence of Leptospirosis among acute febrile illness

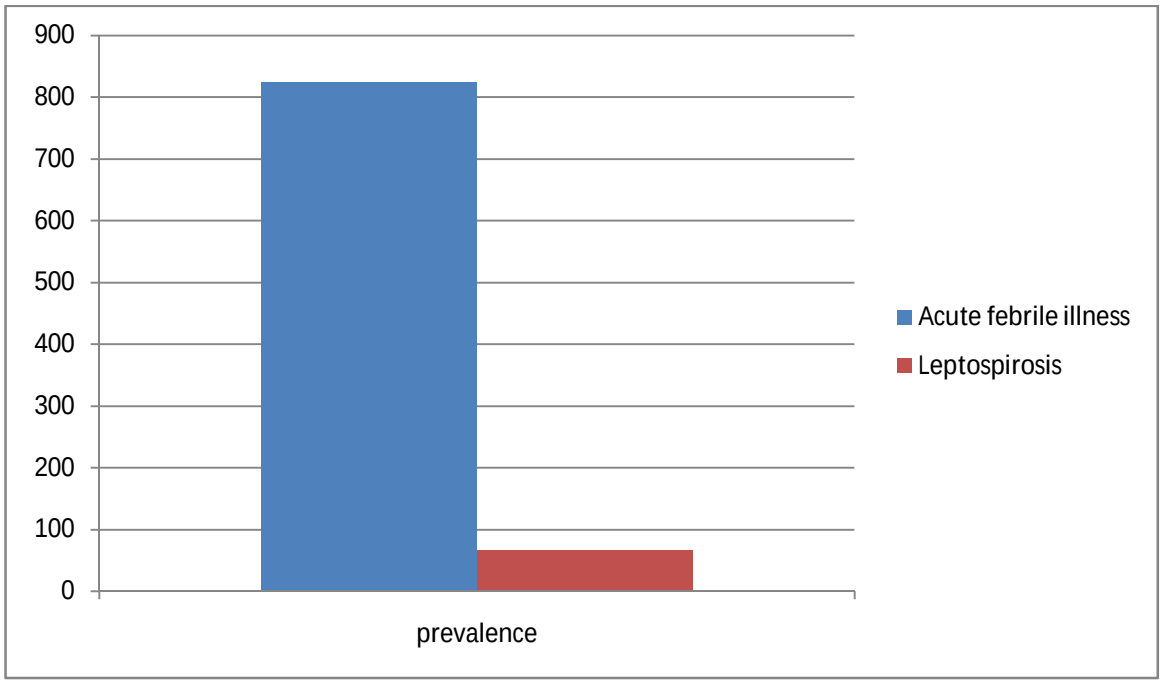
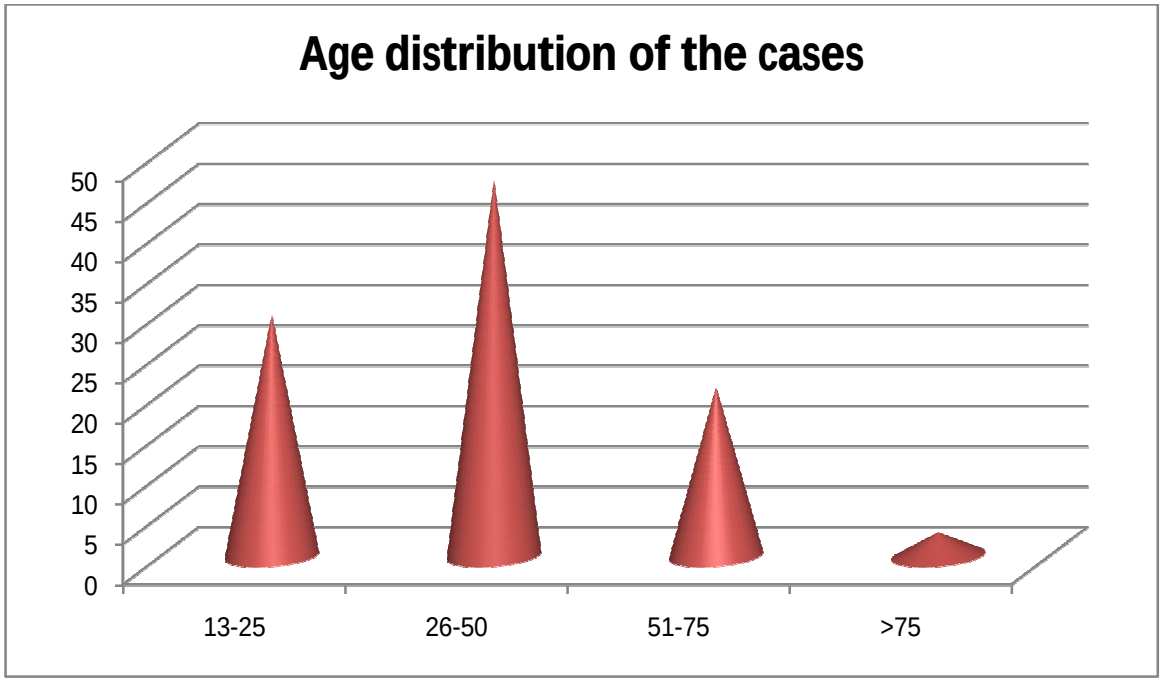


Table no 2: Age distribution of the cases

Age group	Number	Percentage
13-25	20	29.8
26-50	31	46.5
51-75	14	20.8
>75	2	2.9
Total	**67**	**100**

Graph no 2: Age distribution of the cases

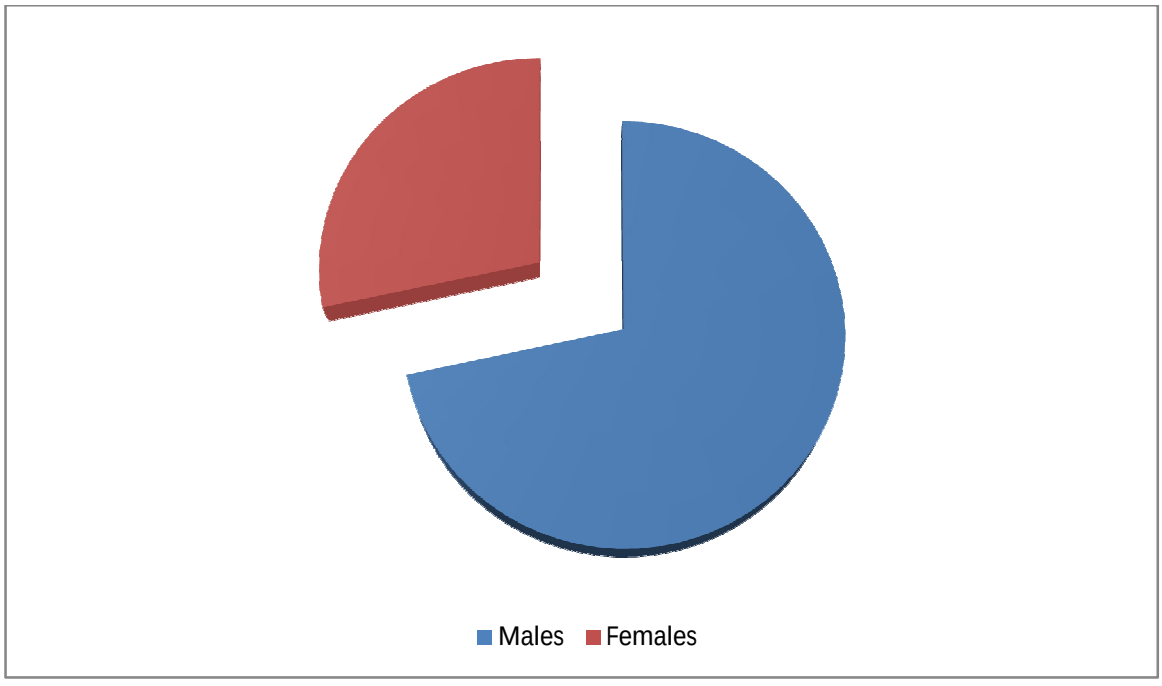


Out of 67 cases, 31 cases (46.5%) belonged to the age group 26-50 years which constituted the majority, followed by 20 cases (29.8%) in the age group 13-25 years, followed by 14 cases (20.8%) in the age group 51-75 years and 2 cases above 75 years of age, constituting 2.9%. p value was 0.0001, which is significant ($p<0.05$).

Table no 3: Sex distribution of the cases

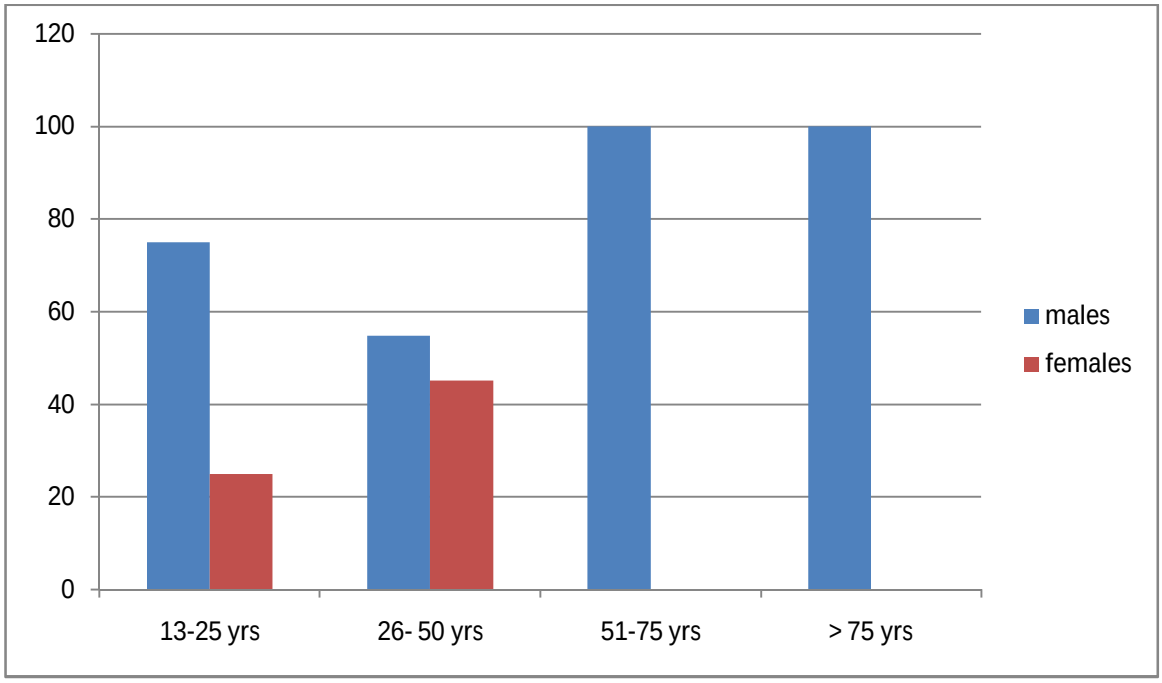
Sex	Number	Percentage
Male	48	71.6%
Female	19	28.4%
Total	**67**	**100**

Graph No 3: Sex distribution of the cases



Among the 67 cases, males were majority constituting 71.6% (n=48) followed by females constituting 28.4% (n=19). Male : female ratio was noted to be 2.5:1. There was a significant difference between the gender according to p value which was < 0.0001 ($p<0.05$).

Graph no 4: Age and sex distribution of the cases

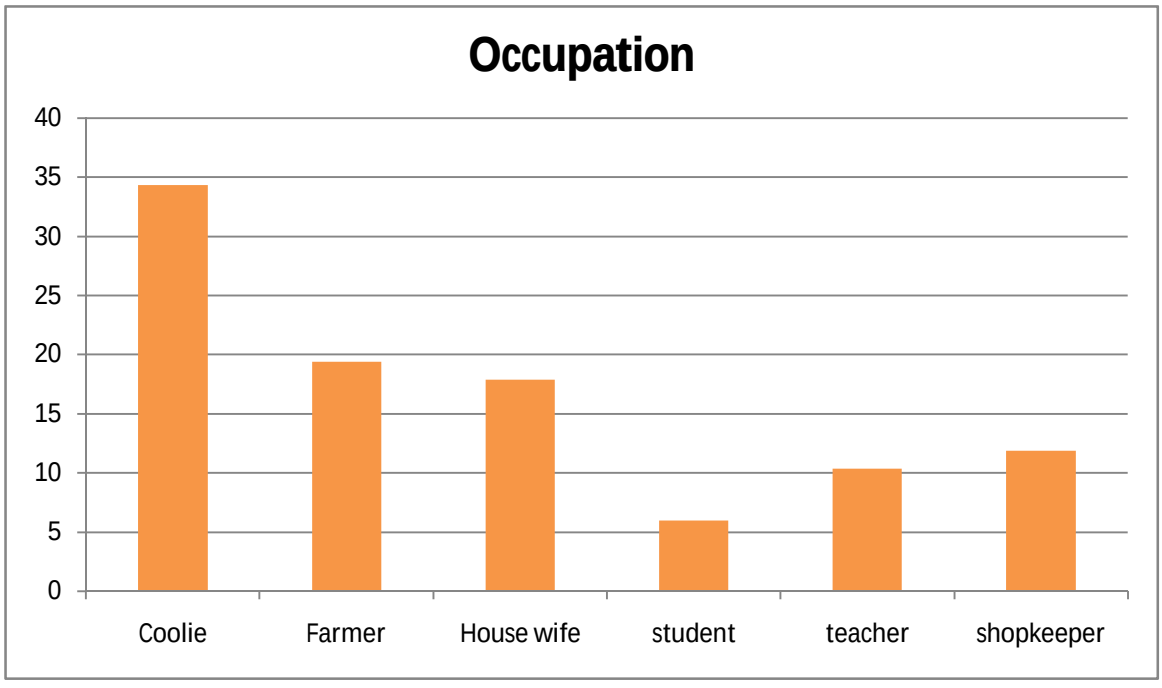


No females in the age > 50 years were encountered in the study. Majority of the females belonged to the age group 26-50 years (n=14) followed by 13-25 years (n=5).

Table no 4: Occupation

Occupation	No of cases	Percentage %
Coolie	23	34.3
Farmer	13	19.4
House wife	12	17.9
Student	4	6
Teacher	7	10.4
Shopkeeper	8	11.9
Total	**67**	**100**

Graph no 5: Occupation

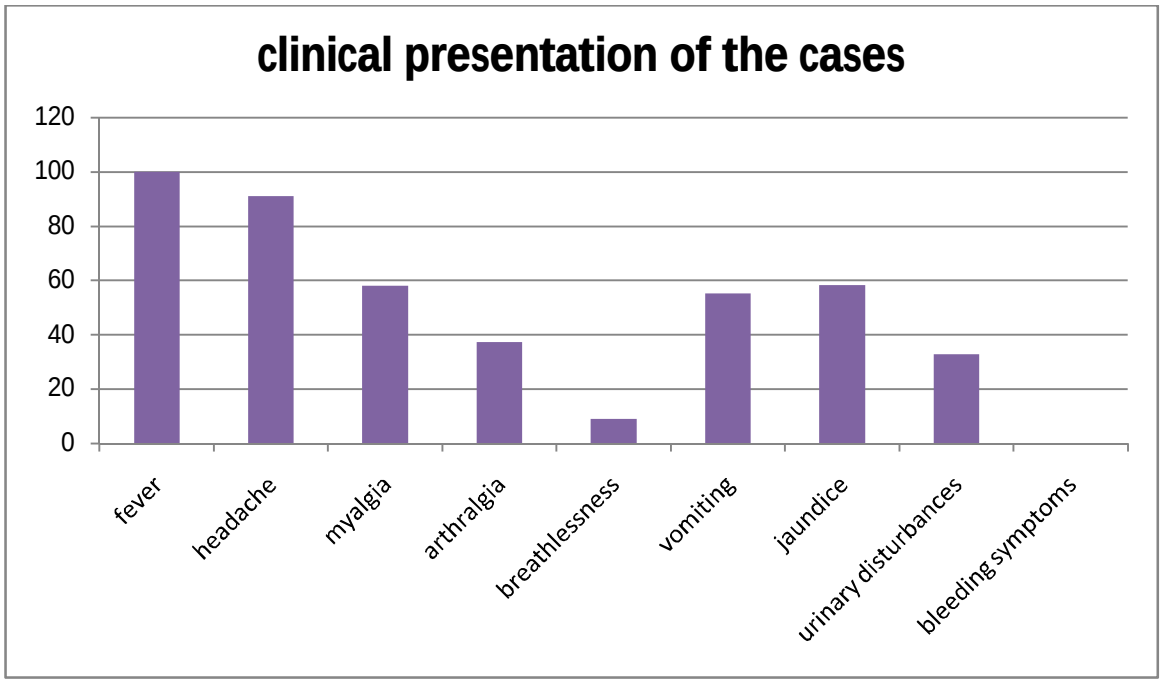


Out of 67 cases, 23 cases were coolie, constituting the majority (34.3%), followed by 13 cases of farmers, constituting 19.4%, house wives were 12 cases, constituting 17.9%, shopkeepers were 8 in number, constituting 11.9%, 7 cases were teachers, constituting 10.4%, 4 cases were students, constituting 6%. P value was 0.0001 which was significant ($p<0.05$).

Table no 5: Clinical presentation of the cases

Symptoms	No of cases	Percentage
Fever	67	100 %
Headache	61	91%
Myalgia	58	86.6%
Arthralgia	25	37.3
Breathlessness	6	8.9
Vomiting	37	55.2
Jaundice	39	58.2
Urinary disturbances	22	32.8
Bleeding symptoms	6	8.9

Graph no 6: clinical presentation of the cases



Fever was the most common symptom, seen in all cases, constituting 100%.Headache was the next common symptom seen in 61 cases, constituting 91%, followed by myalgia seen in 58 cases, constituting 86.6%, followed by jaundice in 39 cases, constituting 58.2%, vomiting in 37 cases, constituting 55.2%, arthralgia in 25 cases, constituting 37.3%.

Urinary disturbances were seen in 22 cases, constituting 32.8%. All the cases had oliguria.

Bleeding symptoms were seen in 6 cases, constituting 8.9%. 4 cases had hematuria as the bleeding symptom and ecchymosis was seen in 2 cases.

Among the 67 cases, 40 patients had fever of duration between 6-10 days constituting 59.7%, followed by 17 patients with duration between 11- 15 days, constituting 25.4% and 10 cases with fever duration between 1-5 days, constituting 14.9%. p value was 0.0001, which is significant ($p<0.05$).

Graph no 7: Duration of fever

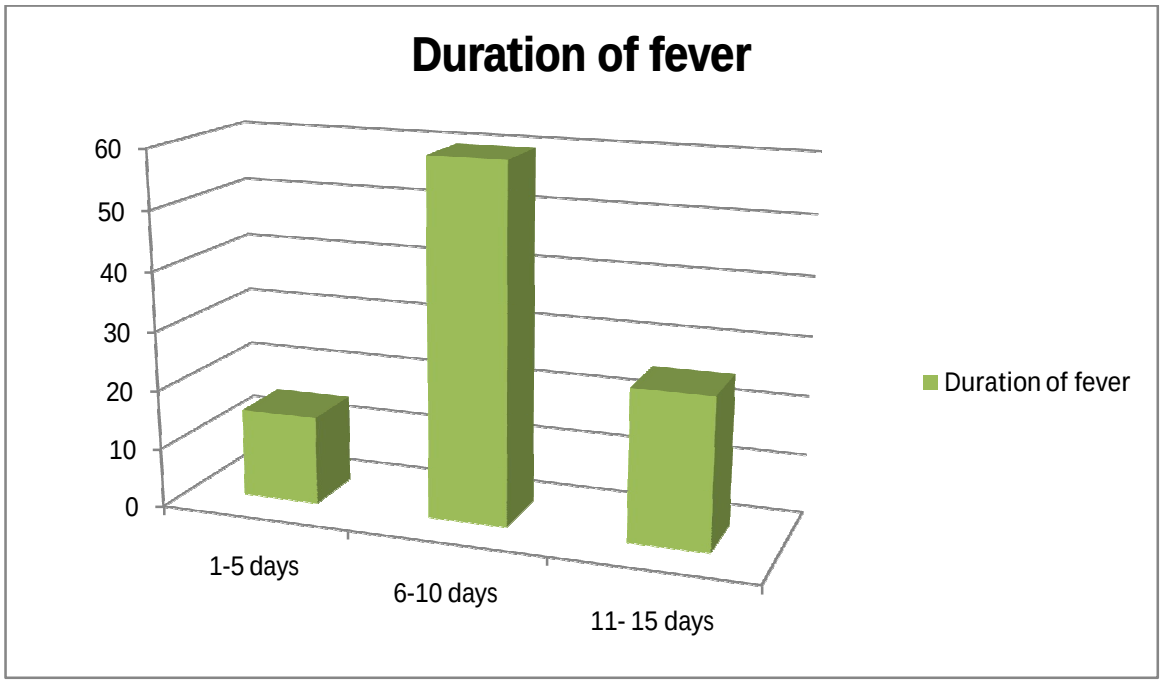
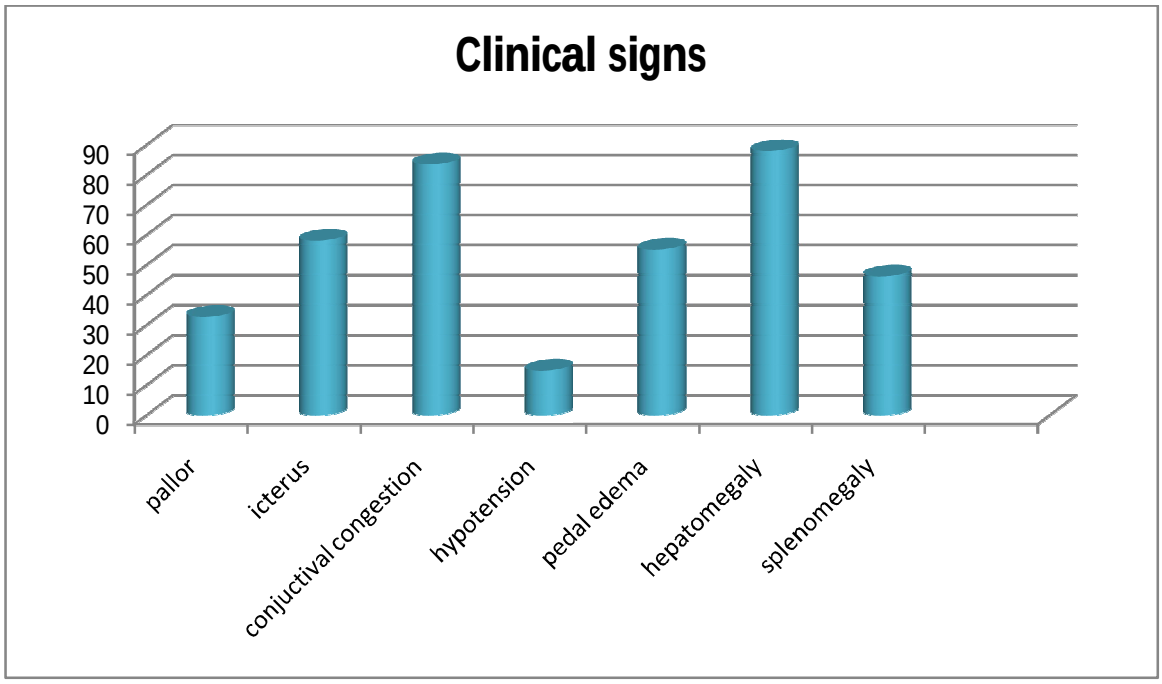


Table no 6: Clinical signs

Signs	No of cases	Percentage %
Pallor	22	32.8 %
Icterus	39	58.2%
Conjuctival congestion	56	83.6%
Hypotension	10	14.9%
Pedal edema	37	55.2%
Hepatomegaly	59	88%
Splenomegaly	31	46.3%

Graph no 8: Clinical signs



Most common clinical sign was hepatomegaly, seen in 59 cases, constituting 88%, followed by conjuctival congestion, seen in 56 cases, constituting 83.6%, followed by icterus seen in 39 cases, constituting 58.2%, pedal edema seen in 37 cases, constituting 55.2%, splenomegaly seen in 31 cases, constituting 46.3%, pallor seen in 22 cases, constituting 32.8% and hypotension seen in 10 cases, constituting 14.9%. p value was 0.0001, which is significant ($p<0.05$).

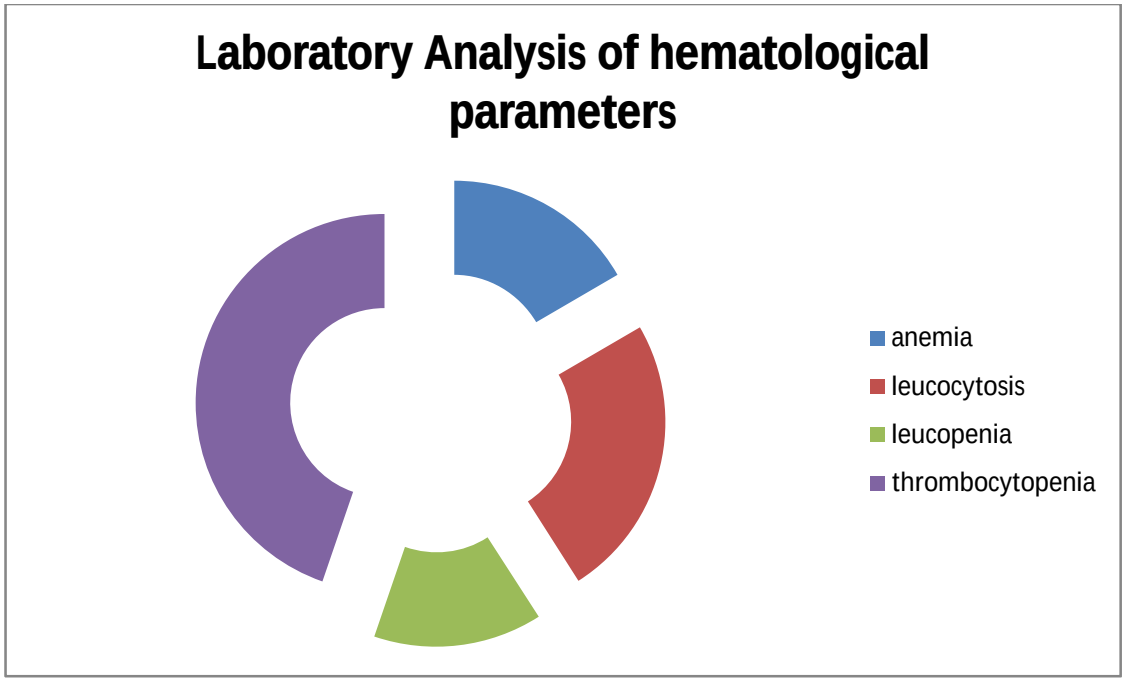
Among the 67 cases, 6 cases (8.9%), developed ARDS and 2 cases (3%) developed myocarditis.

LABORATORY ANALYSIS OF BLOOD COUNTS

Table no 7: Laboratory Analysis of hematological parameters

Parameters	No of cases	Percentage
Anemia	22	32.8%
Leucocytosis	32	47.8%
Leucopenia	19	28.4
Thrombocytopenia	59	88%

Graph no 9: Laboratory Analysis of hematological parameters

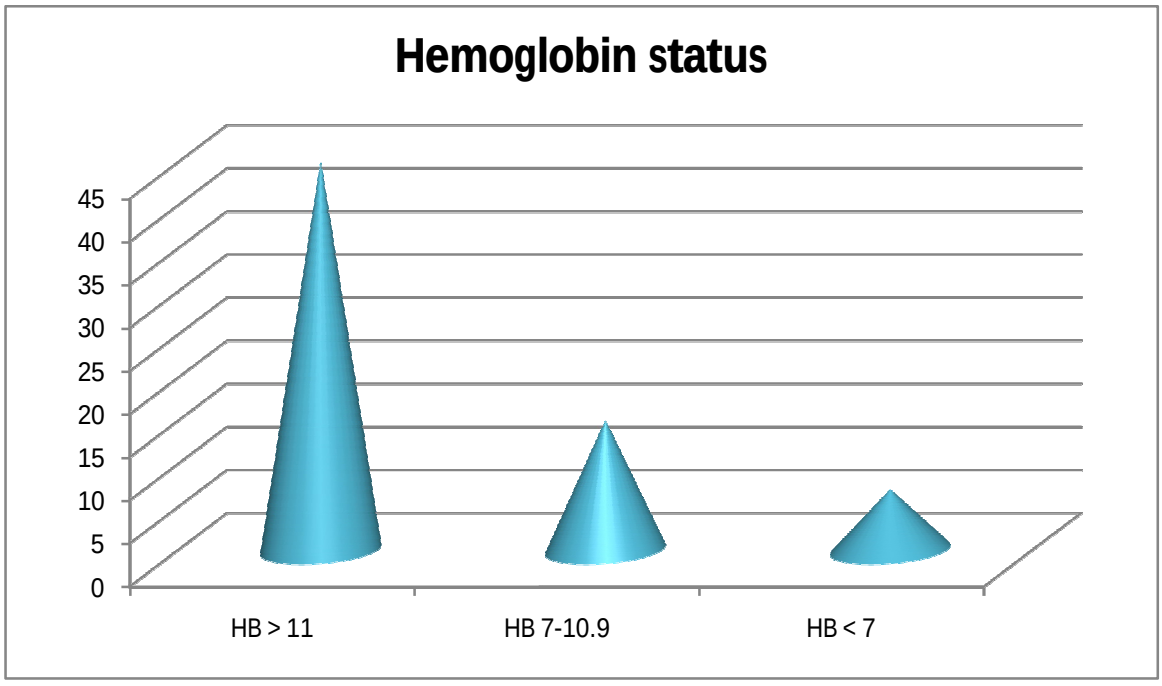


Among the laboratory parameters, thrombocytopenia constituted the majority seen in 59 cases, accounting for 88%. p value was found < 0.0001, which is significant ($p<0.05$)

Table No 8: Distribution of the cases with anemia

Hemoglobin	**No of cases**	**Percentage %**
7-10.9 gms%	15	68%
< 7 gms%	7	32%
Total	**22**	**100%**

Graph no 10: Distribution of the cases with anemia



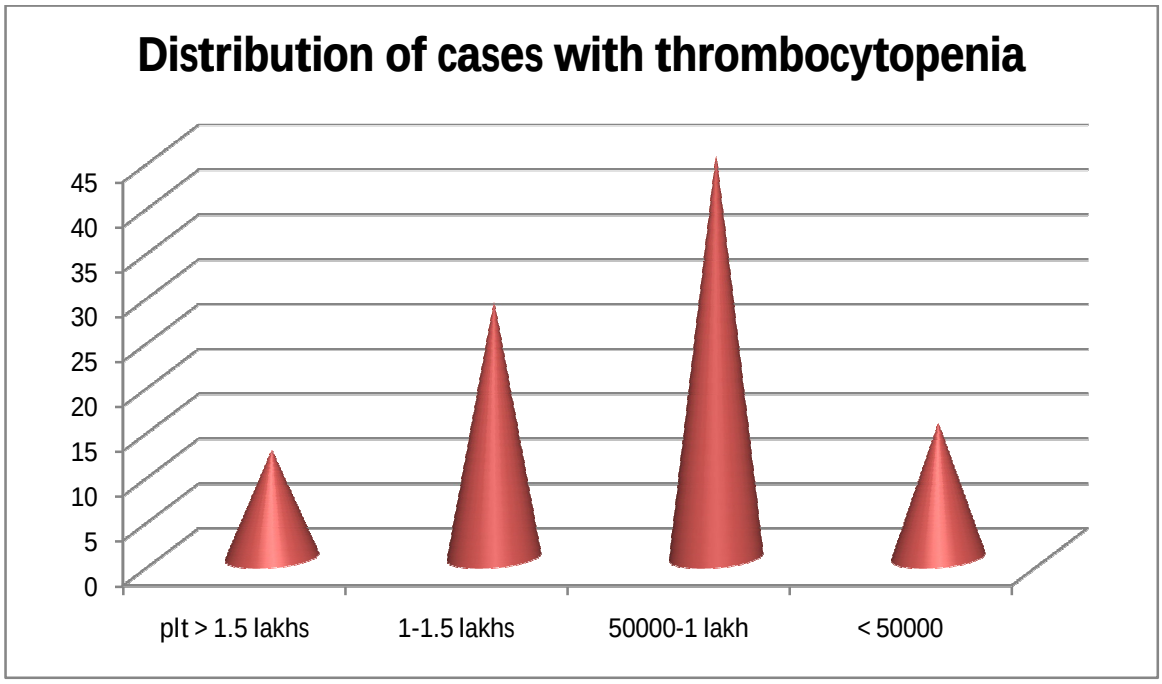
Hemoglobin was more than 11gms%, seen in 45 cases, constituting 67.1%. Anemia was seen in 22 cases, constituting 32.8%. All the 22 cases had hemoglobin less than 11gms%. p value was 0.0007, which is significant (<0.05).

Out of the 22 cases with anemia, 15 cases had hemoglobin between 7-10.9 gms%, constituting 68% and 7 cases had hemoglobin below 7gms%, constituting 32%.

Table no 9: Distribution of the cases with thrombocytopenia

Platelet count	No of cases	Percentage
1- 1.5 lakhs	19	32.2%
50000- 1 lakh	30	51%
< 50000	10	16.8%
Total	**59**	**100**

Graph no 11: Distribution of the cases with thrombocytopenia



Platelet count was more than 1.5 lakhs, seen in 8 cases, constituting 11.9%. Thrombocytopenia was seen in 59 cases, accounting for 88% (p value < 0.0001). Out of the 59 cases, 30 cases had platelet count between 50000- 1 lakh, constituting 51%, 19 cases had platelet count between 1-1.5 lakhs, constituting 32.2% and 10 cases had platelet less than 50000, constituting 16.8%.

LABORATORY ANALYSIS OF RENAL FUNCTION TESTS:

Table No 10: Distribution of the cases according to serum urea

	No of cases	**Percentage**
Urea < 40mg/dl	27	40%
Urea > 40mg/dl	40	60%
Total	**67**	**100**

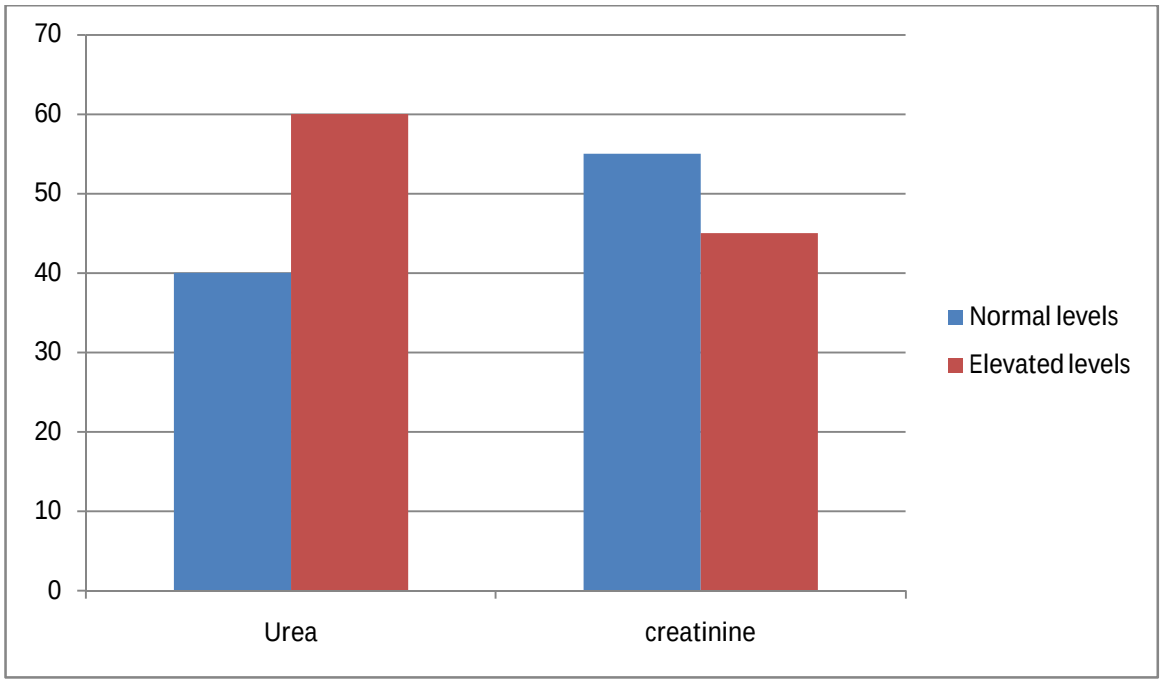
Out of the 67 cases, 40 cases had urea more than 40mg/dl, constituting 60%. Maximum value of elevated serum urea encountered was 298 mg/dl. p value was 0.0455 which was significant (<0.05).

Table no 11: Distribution of the cases according to serum creatinine

	No of cases	Percentage
Creatinine < 1.4mg/dl	37	55
Creatinine > 1.4mg/dl	30	45
Total	**67**	**100**

Out of the 67 cases, 30 cases had creatinine more than 1.4mg/dl, constituting 45%. The maximum value of serum creatinine encountered in the present study was 11mg/dl. p value was 0.3173, which was not significant (i.e > 0.05).

Graph no 12: Laboratory analysis of renal function tests



Out of the total 67 cases, serum urea was found elevated in majority of cases (60%) when compared to serum creatinine(40%).

LABORATORY ANALYSIS OF LIVER FUNCTION TESTS

Out of 67 cases, 48 cases had total bilirubin more than 1.1mg/dl, constituting 71.6%. In 19 cases (28.4%), serum total bilirubin was normal, less than 1.1 mg/dl. The maximum value of serum total bilirubin observed was 15.2mg/dl. Majority of the cases had serum total bilirubin more than 7 mg/dl (56.2%). p value was 0.0030, which is significant (i.e < 0.05)

Table no 12: Distribution of the cases according to serum total bilirubin

Serum total bilirubin	No of cases	Percentage%
1.11 – 3 mg/dl	9	18.8
3.1-7 mg/dl	12	25
>7 mg/dl	27	56.2
Total	**48**	**100**

Out of 67 cases, 54 cases had direct bilirubin more than 0.2mg/dl, constituting 80.6%. In 13 cases (19.4%), serum direct bilirubin was normal, less than 0.2mg/dl. The maximum value of serum direct bilirubin observed was 9.8mg/dl. Majority of the cases had serum direct bilirubin

between 2.1- 5 mg/dl (50%). p value was 0.0242, which is significant (i.e < 0.05)

Table no 13: Distribution of the cases according to serum direct bilirubin

Serum direct bilirubin	No of cases	Percentage%
0.21-2 mg/dl	16	30
2.1-5 mg/dl	27	50
>5 mg/dl	11	20
Total	**54**	**100**

Out of 67 cases, 48 cases had serum SGOT more than 40 u/l, constituting 71.6%. In 19 cases (28.4%), serum SGOT was normal, less than 40 u/l. The maximum value of serum SGOT observed was 860 u/l. Majority of the cases had serum SGOT more than 450 mg/dl (54.1%). p value was 0.0072, which is significant (i.e < 0.05).

Table no 14: Distribution of the cases according to serum SGOT

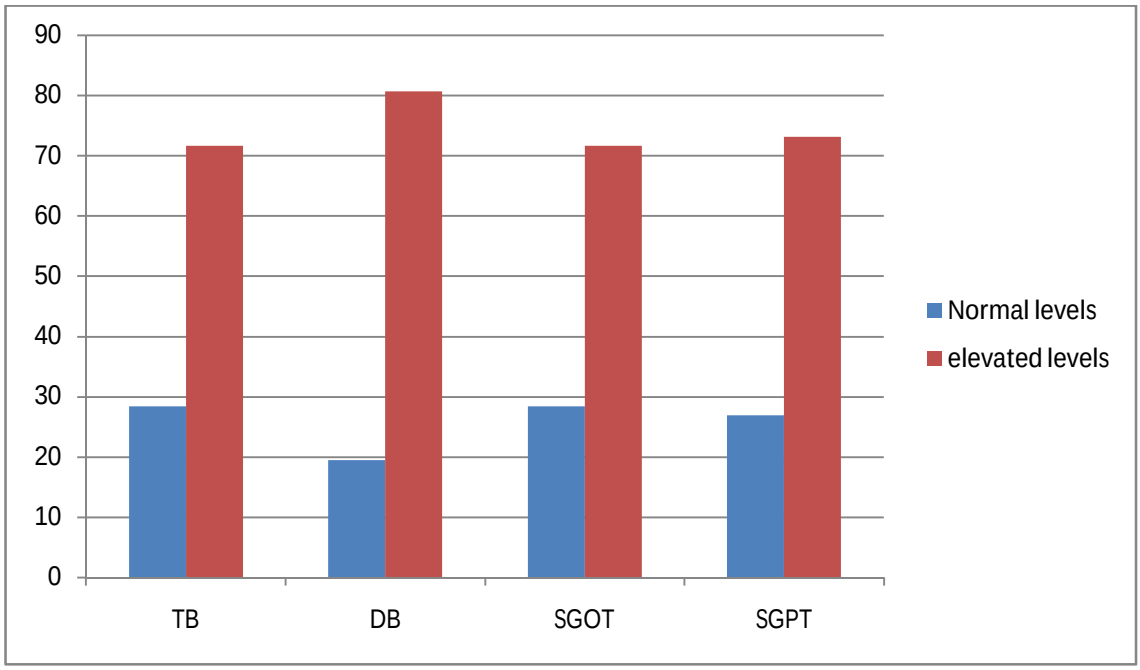
Serum SGOT (u/l)	No of cases	Percentage %
41-150	9	18.8
151-450	13	27.1
451-900	26	54.1
Total	**48**	**100**

Out of 67 cases, 49 cases had serum SGPT more than 40 u/l, constituting 73.1%. In 18 cases (26.9%), serum SGPT was normal, less than 40 u/l. The maximum value of serum SGPT observed was 898 u/l. Majority of the cases had serum SGPT more than 450 mg/dl (49%). p value was 0.0442, which is significant (i.e < 0.05)

Table no 15: Distribution of the cases according to serum SGPT

Serum SGPT (u/l)	No of cases	Percentage %
41-150	10	20.4
151-450	15	30.6
451-900	24	49
Total	**49**	**100**

Graph no 13: laboratory analysis of liver function tests

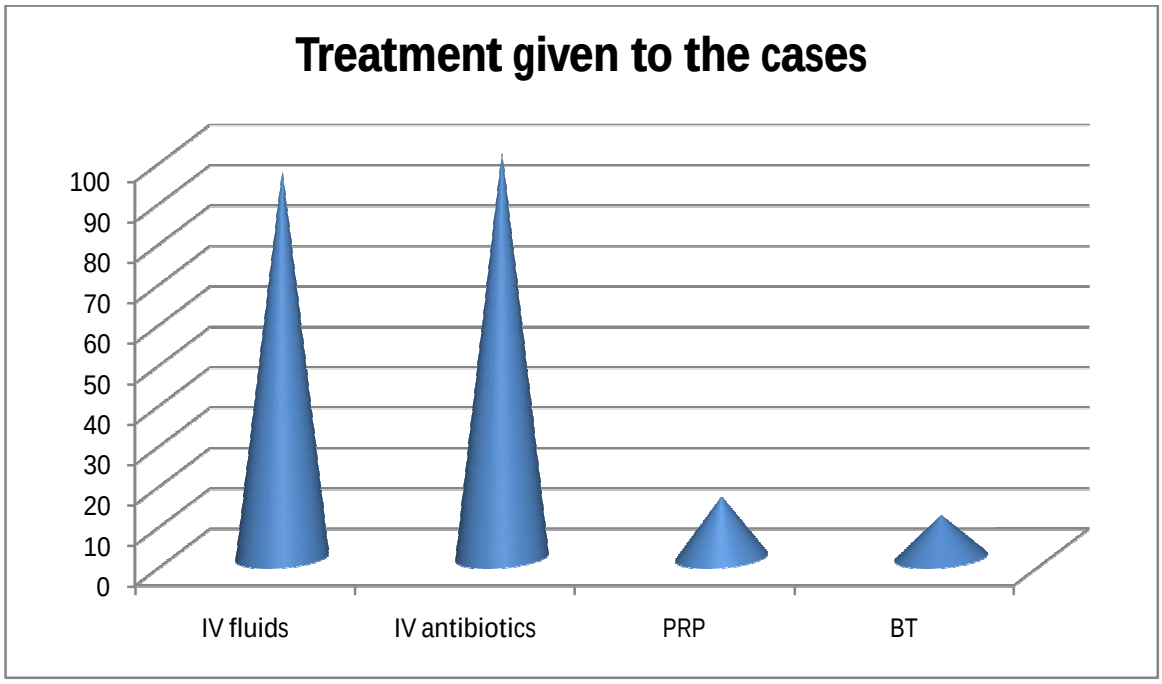


Among all the parameters of liver function tests, serum direct bilirubin was found to be elevated in majority of cases (n=54), constituting 80.6%.

TREATMENT OF THE CASES: Table no 16: Treatment given to the cases

Treatment	**No of cases**	**Percentage %**
IV Fluids	64	95.5
Antibiotics	67	100
Platelet rich plasma (prp)	10	15
Blood transfusion (BT)	7	10.4

Graph no 14: Treatment given to the cases



General treatment with intravenous fluids was given in 64 cases, constituting 95.5%.Specific treatment with Antibiotics was given in all cases (100%). Majority of the patients, 51 patients were given IV penicillin (76.1%). 16 cases, who had mild symptoms and no complications were given oral Doxycycline (23.9%).

Platelet rich plasma was administered in 10 cases, constituting 15%. All the 10 cases had platelet count less than 50000. Out of the 10 cases with platelet count less than 50000, 6 cases had bleeding symptoms, constituting 60%. Bleeding was encountered in form of hematuria, seen in 4 cases, constituting 66.7% out of the 6 cases and eccymosis seen in 2 cases, constituting 33.3%.

Blood transfusion was carried out in 7 cases, constituting 10.4%. All the 7 cases had hemoglobin less than 7gms%.

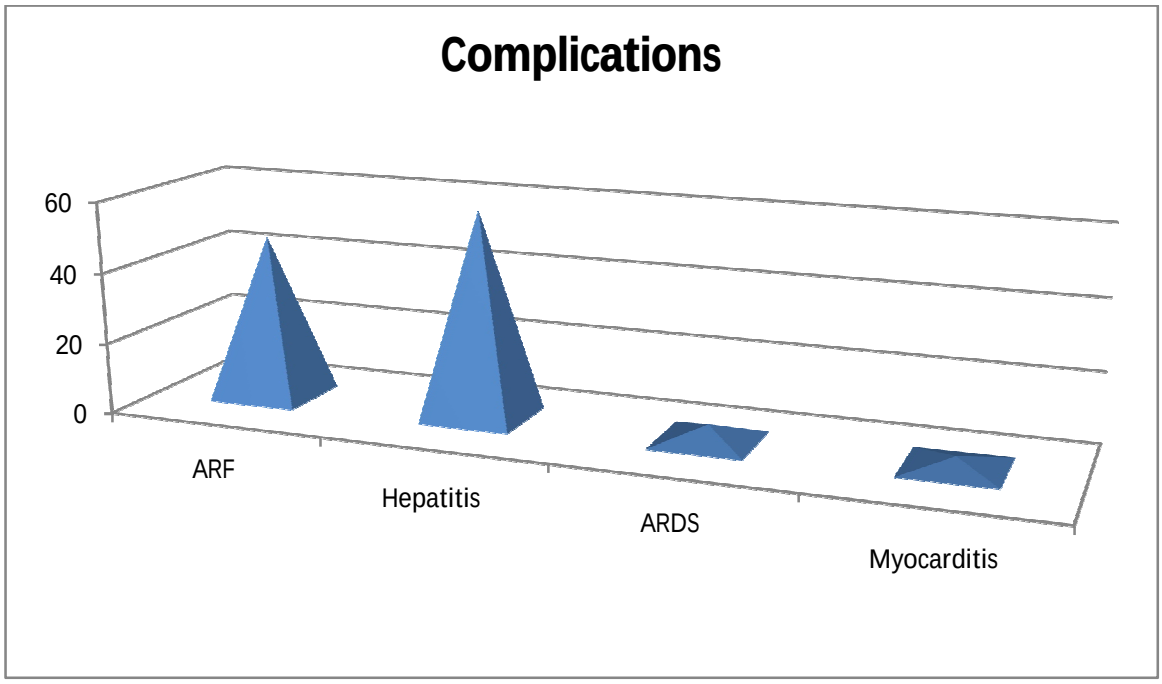
COMPLICATIONS

Out of 67 cases, 51 cases (76.1%) developed complications during the hospital stay. 16 cases had no complications, constituting 23.9%.

Table no 17: complications

Complication	No of cases	Percentage %
Acute renal failure (ARF)	31	46.3
Hepatitis	39	58.2
ARDS	3	4.5
Myocarditis	2	3

Graph no 15: complications



Hepatitis was the most common complication encountered, seen in 39 cases, constituting 58.2%. ARF was the next common complication, seen in 31 cases, constituting 46.3%. ARDS was seen in 6 cases, constituting 8.9%. Myocarditis was the least common complication encountered seen in 2 cases, constituting 3%. p value was less than 0.0001, which is significant.

Intubation and mechanical ventilation was done in 2 cases, out of 3 cases of ARDS, constituting 66.6%.

Dialysis was carried out in 17 patients of ARF, out of 31 cases, constituting 54.8%.

24 cases had more than one complication, accounting for 35.8% of the total 67 cases.

Table no 18: Combined complications

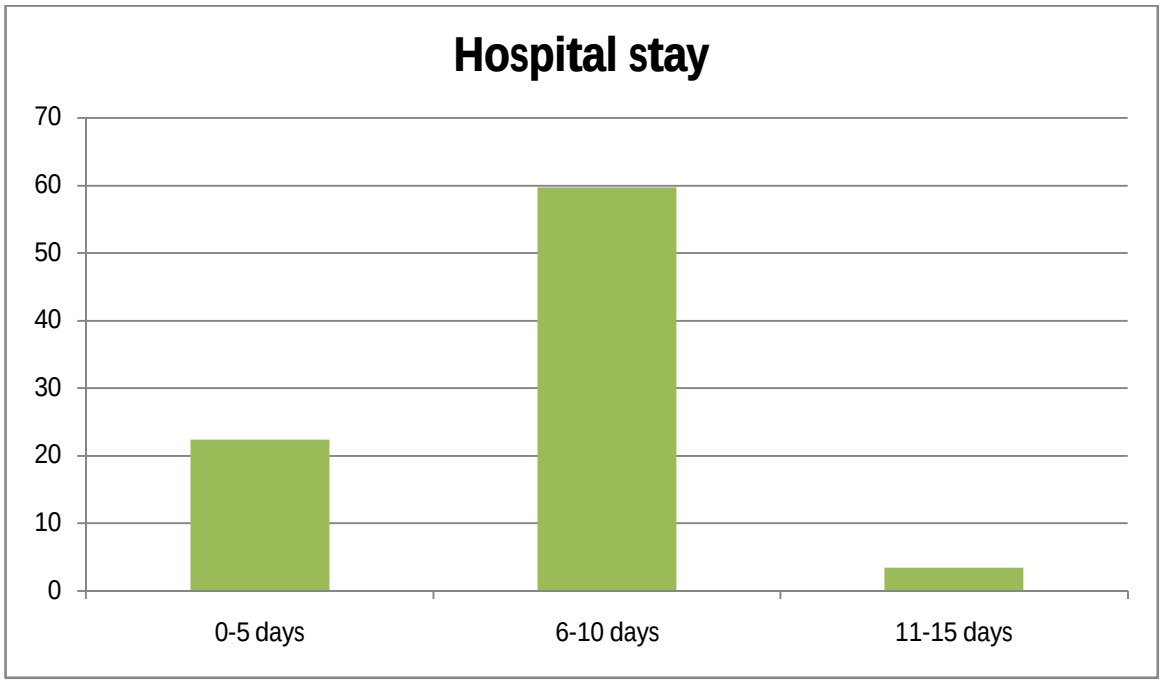
Combined complications	No of cases	Percentage %
ARF + Hepatitis	22	91.7
ARDS + Hepatitis	2	8.3
Total	**24**	**100**

HOSPITAL STAY

Table no 19: Hospital stay

No of days of hospital stay	Number	Percentage
0-5 days	15	22.4
6-10 days	40	59.7
11-15 days	12	17.9
Total	**67**	**100**

Graph no 16: Hospital stay



Majority of the cases (n=40) had hospital stay between 6-10 days, constituting 59.7%, followed by 15 cases between 0-5 days, constituting 22.4%, 12 cases had hospital stay between 11-15 days, constituting 17.9%. Longer duration of the hospital stay was seen in patients who had complications.

MORTALITY :

Out of 67 patients, 3 patients died, constituting 4.5%. 2 cases died due to acute renal failure. One case had both hepatitis and ARDS and died.

DISCUSSION

Apart from being a rural disease affecting the farmers in particular,Leptospirosis in the modern times has become an urban endemic.It has been on the rise in states like Karnataka and Tamil Nadu contributed by increased cultivation and inadequate vector control.

Hence this study was taken up in Kilpauk Medical College Hospital,mainly nurturing the urban population within the city limits.The primary aim was to analyse the clinical profile of the disease and the pattern of multiorgan involvement.Totally 67 proven cases of leptospirosis admitted to Kilpauk medical College during a period of 8 months were involved in the study.

Out of the 824 fever cases admitted during the study period leptospirosis constituted 8.1% (67 cases).Among those admitted males constituted 71.6% and females 28.4% with the ratio being 2.5:1.

Regarding occupation,34.3% of the cases were coolie followed by farmers accounting for 19.4%.This clearly indicates the incidence of the disease is very high among outdoor manual working population and farmers.(53.7% combined together).A similar study by Muthusethpathi et al during 1990 in Madras showed an incidence of 59 % in outdoor workers.This correlates with the natural epidemiology of the disease.

Analysing the presenting symptoms fever was the universal presenting symptom present in all the cases studies (100%) followed by headache (91%),myalgia (86.6%) and jaundice (58.2%).In a similar study by Elizabeth .F. Daher et al in the metropolitan city of Fortaleza in Brazil,the main symptoms included fever (94.7%),myalgia (92%),Jaundice (94%),Headache (74%).Oliguria was found in 32.8% (24 cases).In the same study by Daher showed there is significant mortality in patients presenting with oliguria than the non-oliguric cases.Among the 3 cases who died due to Leptospirosis 2 cases had Oliguric renal failure constituting 66% to mortality.

Among the 31 cases (46%) presenting with ARF,dialysis was needed in 17 patients (54.8 %),thus reflecting Acute Renal Failure particularly non oliguric as a grave prognostic sign.In western population,the incidence of renal failure was around 70-80 % in various studies but whereas in Indian setup it varies from 40-60%.

Conjuctival suffusion was observed in 56 cases (83.6%).The 1990 madras studies had only 59 % having conjuctival signs but the western literature shows higher incidence (70-80%),thus making conjuctival suffusion as a reliable clinical diagnostic marker of the disease.

The study showed hepatomegaly in 59 cases (81%) and splenomegaly in 31 cases (46.3%).Soth American studies by

Rafael,Geraldo et al showed lesser incidence of hepatomagaly (37%) and Splenomegaly (21%)

Analysing the hematological parameters,thrombocytopenia constituted the majority accounting for 88% (totally 59 cases) with a significant p value of <.05.In the Madras study 30% had lower platelets with 26 % having evidence of internal bleeding contributing to morbidity.

Abnormal liver function tests were found in 71.6% (48 cases).The notable abnormalities were significant direct hyperbilirubinemia (80.6%) ($p < 0.05$).In a similar study by Tatitanawat & Tanjatham et al a total bilirubin of >2.5mg/dl was an independent risk factor for mortality.The Madras study showed 84.7% of patients having high Bilirubin and altered AST and ALT.In this study 48 cases (76%) had AST > 40 u/L with the maximum being 860 u/L.73 % had high ALT with the maximum being 898 u/L.The study by Jaureguiberry et al found abnormal AST and ALT in 83 and 86 % respectively with mean AST and ALT higher in nonsurvivors when compared to survivors of the disease.

Metabolic acidosis and ARDS was noted in 3 cases (4.5%) with 1 death out of total 3 due to respiratory complication.

Among the 67 patients admitted 95.5 % received general treatment with intravenous fluids and specific treatment with IV Penicillin for

moderate to severe cases (76.1%) and milder uncomplicated cases were treated with oral Doxycycline (23.9%).Blood transfusion was needed in 7 cases (10.4%) who had anemia,thrombocytopenia and bleeding manifestations.

CONCLUSION

- Leptospirosis was found to be common in outdoor manual workers and farmers (53%)
- Males are at high risk due to occupational exposure (71%) the sex ratio being 2.5:1
- The most common observed symptom was Fever (100%) Headache (91%) and Myalgia (86.6%)
- Conjuctival suffusion was found in 83.6% of patients
- Hepatomegaly was found in 88% patients and spenomegaly was found in 46.3%
- Anemia was found in 32.8%
- Thrombocytopenia was present in 88% cases
- Bleeding manifestations were found in 8.9%
- 58.2% had reversible hepatic damage
- 4.5 % patients developed ARDS.
- 46.3% patients developed ARF.
- Crystalline Penicillin iv was the drug of choice in moderate to severe leptospirosis
- 4.5% died due to complications

SUMMARY

The main aim of the study being analyzing the clinical profile of Leptospirosis in a suburban population,this work was carried out in Kilpauk medical College Hospital and a total of 67 cases were admitted and analysed

The incidence of the disease was found to be 8.1% among the fever cases admitted in KMCH adding to the fact that Chennai is a proven endemic area for Leptospirosis.

In the study leptospirosis was eventually found to be more common among the agriculturists and outdoor workers,particularly males the ratio being 3:1.the most common age of incidence was between 26-50 years

Regarding the symptomotology the notable were fever (100%),headache (91%) and myalgia (86.6%).urinary disturbances were seen in 32.8%.

The most common clinical signs were conjuctival congestion (83.6%),Hepatomegaly (88%) followed by Icterus(58.2%).CNS and Respiratory involvement signs were associated with bad prognosis.

Among the laborotary investigations,there was high incidence of Thrombocytopenia (88%) followed by leucocytosis (47.8%) and Anemia

(32.8%).serum bilirubin was high in 48 cases (71.6%).The direct fraction was more in 80.6%.Notable among the Liver enzymes,was increase in ALT and AST in 73% and 71.6% respectively.there was also a significant increase in serum ALP in 28% of cases.

Crystalline penicillin given intravenously for one week was found to be the satisfactory drug of choice for most of the cases(76.1%).For milder cases oral Doxycycline (23.9%) 100mg given twice daily for one week was tried with similar success rate

Among the 67 patients included in the study 16 cases (23.9%) had no complications whereas 76%(51 cases) developed various complications.Notable among them was ARF (46.3%),Hepatitis(58.2%).The occurrence of myocarditis was rare(3%).The majority duration of hospital stay was 6-10 days(59.7%)

Thus leptospirosis proves to be an important health problem in Indian subcontinent particularly the southern states and hence early diagnosis and initiation of treatment is important in preventing morbidity and mortality.

More emphasis should be laid on preventive measures that would decrease the incidence of the disease.

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ANNEXURE

PROFORMA

TITLE OF THE TOPIC :

"CLINICAL PROFILE OF LEPTOSPIROSIS WITH SPECIAL REFERENCE TO MULTI ORGAN INVOLVEMENT IN KILPAUK MEDICAL COLLEGE"

I) Patient Details:

Name:	I.P. No.
Age:	Address:
Sex:	Occupation:
Date of admission:	Date of discharge:

II) PRESENTING COMPLAINTS: Duration

1) Fever Yes/No. ( )
2) Headache Yes/No. ( )
3) Retroorbital pain Yes/No. ( )
4) Back ache Yes/No. ( )
5) Myalgia Yes/No. ( )
6) Arthralgia Yes/No. ( )
7) Maculo papular rash Yes/No. ( )
8) Pain abdomen Yes/No. ( )
9) Vomiting Yes/No. ( )
10) Jaundice Yes/No. ( )
11) Urinary disturbances-oliguria Yes/No. ( )
12) Sore throat Yes/No. ( )
13) Cough Yes/No. ( )
14) Breathlessness Yes/No. ( )
15) Rhinitis Yes/No. ( )
16) Diarrhoea Yes/No. ( )
17) Convulsions Yes/No. ( )
18) Photophobia Yes/No. ( )
19) Altered sensorium Yes/No. ( )
20) Bleeding manifestations - epistaxis Yes/No. ( )
    - Haematamesis Yes/No. ( )
    - Malena Yes/No. ( )
    - Hypermennorrhoea Yes/No. ( )
    - Haematuria Yes/No. ( )
    - Haemoptysis Yes/No. ( )
21) Bilateral conjuntival suffusion Yes/No. ( )
22) Any other symptoms Yes/No. ( )

III) History of present illness:

1) **Fever** :
   a) Duration
   b) Degree: Mild/Moderate/High
   c) Type:
   Intermittent/continuous/remittent
   d) Associated feature:
   Chills/Rigors/sweating

2) **Headache**:
   a) Duration
   b) Unilaterally/bilateral/diffuse
   c) Nature
   d) Associated features

3) **Vomiting**:
   a) Duration
   b) Frequency
   c) Projectile/non-projectile

4) **Altered sensorium**:
   a) Duration
   b) Behaviour
   c) Intelligence
   d) Memory: Past/Present
   e) Orientation to time, place and Person
   f) Speech

5**) Loss of consciousness** :
   Glas gow coma scale

6**) Convulsion**:
   a) Duration/aura
   b) Focal/generalized

IV) Past History:

V) Treatment History:

VI) Family History:

VII) Personal History:

VIII) Environmental History:Incidence of leptospirosis in the area of residence.

IX) Occupation History:

X) General physical Examination:

Built -
Nourishment

Pallor
Icterus
Clubbing

Vital parameters

Pulse……/min
B.P. …….mm Hg
Temperature……°C
Respiratory rate……/min

Cyanosis
Lymphadenopathy
Koilonychia
Oedema
Herpes labialis
Rashes-purpura-Echymosis-Petechiae
Conjunctival suffusion Bilateral/Unilateral

XI) Systemic Examination:

1) **Abdomen**:

Inspection- Shape
Distention
Position of umbilicus
Abdominal movements
Engorged, tortuous veins
Visible pulsations/ peristalsis
Palpation- Tenderness
Guarding
Rigidity
Abdominal girth
Liver- Enlarged/Not enlarged
Spleen-Enlarged/Not enlarged

2) Cardio vascular system

Inspection- Precordial prominence-bulge
Apical Impulse
Parasternal heave
Palpation- Apical Impulse- site-position
And character

Percussion- Cardiac Borders
Auscultation- Heart sounds Murmurs

3) Respiratory System:

Inspection- Respiratory rate/Rhythm/Character
Shape of the chest
Trachea
Chest movement

Palpation- Trachea
Chest expansion
Percussion- Resonant/Impaired/dull

4) Central nervous system:

a) Mental functions:
b) Cranial nerves:
c) Motor system:
d) Cerebellar signs:
e) Optic fluid:
f) Signs of meningeal irritation

5. Investigations:

1.) Complete heamogram:

Hb%.....gm%
TC……cells-cumm
DC: N…
L…
M…
E…
B…
ESR……..mm/hr
Platelet count…lakhs/cumm (before treatment)
Platelet count…lakhs/cumm (after treatment)

2) Urine Examination: Albumin
Sugar
Microscopy- RBC's
Pus cells
Casts

3) RBS:
4) Blood urea…….mg%
5) Creatinine…….mg%
6) Electrolytes: Sodium:
Potassium:
Chloride:

6) **Chest X-ray:**

7) **Ultra sound abdomen:**

8) **Liver function tests:**

10) ECG:

11) Detection of dengue IgM antibodies:

12) HIV antibodies detected by ELISA (if necessary)

13) IgG, IgM antibodies to leptospirosis

14) LP CSF analysis (if necessary)

Albumin:

Glucose:

Chloride:

Cell type:

Cell count:

15) QBC for MP

16) Widal test

17) Weil felix test (if necessary)

18) Liver biopsy (if necessary)

19) Kidney biopsy (if necessary)

20) ABG Analysis (if necessary)

21) SPO2

22) SPUTUM Examination (if necessary)

Final Diagnosis:

Summary:

Treatment:

Response to Treatment:

KEY TO MASTER CHART

M- MALE

F- FEMALE

P- PRESENT

A-ABSENT

BP- BLOOD PRESSURE

TB- TOTAL BILIRUBIN

DB- DIRECT BILIRUBIN

SGOT- SERUM GLUTAMIC OXALOACETIC TRANSAMINASE

SGPT- SERUM GLUTAMIC PYRUVIC TRANSAMINASE

IVF- INTRAVENOUS FLUIDS

Ab- ANTIBIOTICS

BT- BLOOD TRANSFUSION

PRP- PLATELET RICH PLASMA

G- GIVEN

NG- NOT GIVEN

ARF- ACUTE RENAL FAILURE

HP- HEPATITIS

ARDS- ACUTE RESPIRATORY DISTRESS SYNDROME

MC- MYOCARDITIS

NC- NO COMPLICATIONS

SL.no	name	age	sex	occupation	symptoms									clinical features							
					fever	headache	myalgia	arthralgia	Breathlessness	vomiting	jaundice	urinary disturbances	bleeding	temperature	BP	icterus	pallor	conjuctival congestion	pedal edema	hepatomegaly	splenomegaly
1	Gurusamy	34	M	coolie	P	P	P	A	A	A	A	P	A	101 F	130/80	A	A	P	P	A	A
2	SEKAR	21	M	coolie	P	P	P	P	A	A	P	A	P	102 F	140/80	P	P	P	A	P	P
3	Kamala	24	F	house wife	P	P	P	A	A	A	A	P	A	101 F	140/96	A	A	P	P	A	A
4	Prashanth	26	M	student	P	P	P	A	A	A	P	A	A	102 F	128/86	P	A	P	A	P	P
5	Shilpa	15	F	house wife	P	P	P	P	A	A	P	A	A	102 F	120/80	P	A	P	P	P	A
6	Sheela	28	F	coolie	P	P	A	A	A	P	A	A	A	103 F	140/92	A	A	P	A	P	A
7	Poornima	34	F	house wife	P	P	P	P	A	A	P	P	A	102 F	126/98	P	A	P	P	P	P
8	Thangammal	40	F	farmer	P	P	P	P	P	A	A	A	A	101 F	120/80	A	P	P	A	P	A
9	Thangaraj	55	M	teacher	P	P	P	A	A	P	P	A	A	102 F	140/92	P	A	P	P	P	P
10	Sridhar	21	M	coolie	P	P	P	A	A	P	P	A	A	104 F	132/60	P	A	P	A	P	P
11	Muniappan	59	M	farmer	P	P	P	P	A	A	A	P	A	102 F	138/90	A	P	A	P	A	A
12	Fathima	27	F	house wife	P	P	A	A	A	A	P	A	A	102 F	144/86	P	A	P	A	P	P
13	Pichandi	43	M	coolie	P	A	P	A	A	P	A	A	A	100 F	166/90	A	A	P	P	P	A
14	Parameswaran	35	M	shopkeeper	P	P	A	P	A	A	P	A	P	102 F	156/96	P	P	P	A	P	P
15	Pakianathan	36	M	farmer	P	P	P	A	P	P	A	A	A	101 F	150/90	A	A	P	P	A	A
16	Nithya	47	F	teacher	P	P	A	A	A	A	P	A	A	102 F	142/90	P	A	P	P	P	P
17	Suresh	42	M	shopkeeper	P	P	P	P	A	P	P	A	A	101 F	124/82	P	P	P	A	P	A
18	Sheik Ahmed	48	M	shopkeeper	P	A	P	A	A	A	P	A	A	102 F	120/80	P	A	P	P	P	P

19	Pushpa	32	F	house wife	P	P	P	A	A	P	A	P	A	100 F	118/90	A	A	P	P	A	A
20	Kishore	34	M	farmer	P	P	P	P	P	A	P	A	A	102 F	138/90	P	P	A	A	P	P
21	Mariappan	29	M	coolie	P	P	P	P	A	P	P	A	A	102 F	144/86	P	A	P	P	P	P
22	Punith	30	M	coolie	P	P	P	A	A	A	P	A	A	103 F	142/98	P	A	P	A	P	P
23	Anthonymary	34	F	house wife	P	P	P	P	A	P	A	A	A	102 F	156/96	A	A	P	A	P	A
24	Ramesh	22	M	farmer	P	A	P	A	A	A	P	A	P	102 F	150/90	P	P	P	P	P	P
25	Thiagaraj	18	M	student	P	P	P	A	A	P	P	A	A	104 F	142/90	P	A	P	A	P	A
26	Thangappan	34	M	coolie	P	P	P	P	A	A	P	A	A	102 F	90/60	P	P	P	P	P	P
27	Poomalli	45	F	house wife	P	P	P	A	A	P	P	A	A	100 F	120/80	P	A	A	A	P	P
28	Nafees Khan	43	M	coolie	P	P	A	A	A	A	A	A	A	102 F	118/90	A	A	P	P	P	A
29	Praveena	42	F	teacher	P	P	P	P	P	P	P	A	A	101 F	138/90	P	P	P	A	P	P
30	Dhanush	34	M	coolie	P	A	P	A	A	A	A	A	A	102 F	144/86	A	A	P	A	P	A
31	Lavanya	32	F	shopkeeper	P	P	P	A	A	P	P	A	A	102 F	92/54	P	A	P	P	P	A
32	Radhika	40	F	house wife	P	P	P	P	A	P	P	P	P	100 F	156/96	P	P	P	P	P	P
33	Saranya	47	F	house wife	P	P	P	A	A	P	P	A	A	102 F	150/90	P	A	P	A	P	A
34	Vijay	16	M	student	P	P	P	A	A	A	A	P	A	101 F	142/90	A	A	P	P	P	A

	laboratory investigations								treatment						
Sl.no	Total Count	Platelets	Urea	Creatinine	TB	DB	SGOT	SGPT	IVF	Ab	BT	PRP	Complications	Hospital stay	outcome
1	19000	1.1	76	2	0.9	0.2	40	42	G	G	NG	NG	ARF	8	discharged
2	9500	0.3	48	1.1	5.6	2.7	356	425	G	G	NG	G	HP	6	discharged
3	4300	2.1	171	8.7	1.1	0.4	46	49	G	G	G	NG	ARF	11	died
4	16000	1.2	45	0.9	6	4.6	349	410	G	G	NG	NG	HP	8	discharged
5	8800	0.25	100	5.6	7.2	5	267	287	G	G	NG	G	ARF, HP	9	discharged
6	8900	1.3	47	1.1	1.1	0.3	39	40	G	G	NG	NG	NC	5	discharged
7	15500	1.4	76	4.8	6.5	4.2	327	321	G	G	NG	NG	ARF,HP	10	discharged
8	3900	0.21	35	1	1.1	0.1	39	30	G	G	NG	G	NC	5	discharged
9	7800	1.5	78	0.7	4.7	2.2	346	336	G	G	NG	NG	ARF, HP	11	discharged
10	16700	1.25	28	0.7	7.6	3.9	467	456	G	G	NG	NG	HP	8	discharged
11	4200	3.2	79	3.2	1.4	0.3	45	42	G	G	NG	NG	ARF	9	discharged
12	17600	1.15	31	0.9	6.9	3.8	546	559	G	G	NG	NG	HP	6	discharged
13	6300	1.8	42	0.8	1	0.4	34	38	G	G	NG	NG	MC	8	discharged
14	19800	1.32	21	1	7.9	2.9	678	550	G	G	NG	NG	HP	7	discharged
15	3200	0.5	26	1.1	1.1	0.4	40	34	G	G	NG	NG	NC	4	discharged
16	6500	0.65	154	4.5	9	5.4	565	587	G	G	NG	NG	ARF, HP	9	discharged
17	21000	0.54	50	1.2	6	3.6	450	432	G	G	NG	NG	HP	7	discharged
18	19800	2	66	5.8	12.3	7.4	456	460	G	G	G	NG	ARF, HP	10	discharged

19	15600	1.12	75	6	1	0.5	54	49	G	G	NG	NG	ARF	9	discharged
20	3600	0.19	28	0.9	15.2	9.8	860	898	G	G	NG	G	HP, ARDS	11	died
21	9300	1.05	72	5.7	8.7	5.4	345	356	G	G	NG	NG	ARF, HP	12	discharged
22	17400	0.57	30	0.8	9.5	4.6	576	564	G	G	NG	NG	HP	9	discharged
23	9400	1.9	53	0.7	1.1	0.3	32	38	NG	G	NG	NG	NC	4	discharged
24	17300	0.2	69	7.6	11	7.5	780	699	G	G	NG	G	ARF, HP	11	discharged
25	4200	1.4	32	0.9	8.7	6.8	489	440	G	G	NG	NG	HP	8	discharged
26	16200	1.2	70	5.9	6.9	5.7	546	550	G	G	NG	NG	ARF, HP	9	discharged
27	16700	0.27	49	0.7	9.6	4.1	432	430	G	G	NG	G	HP	8	discharged
28	9500	2.1	31	1.1	1.1	0.2	38	40	G	G	NG	NG	NC	5	discharged
29	16400	1.3	34	1.2	6.4	2.9	350	342	G	G	NG	NG	HP, ARDS	11	discharged
30	15800	1.4	33	1	1.1	0.3	40	40	NG	G	NG	NG	NC	6	discharged
31	16200	0.67	64	5.1	6.1	2.1	345	365	G	G	G	NG	ARF, HP	9	discharged
32	9900	0.72	48	0.9	5.9	2	320	350	G	G	NG	NG	HP	7	discharged
33	19200	1.3	25	0.8	7.6	3.2	453	432	G	G	NG	NG	HP	6	discharged
34	3100	2.3	68	6.2	0.9	0.2	42	44	G	G	NG	NG	ARF	9	discharged

35	tamizhselvan	23	M	farmer	P	P	P	P	A	P	P	P	A	102 F	124/82	P	P	P	P	P	P
36	francis	21	M	coolie	P	P	P	A	A	A	A	A	A	102 F	86/60	A	A	A	A	P	A
37	jothy	46	F	coolie	P	P	P	A	A	P	P	P	A	102 F	118/90	P	A	P	P	P	P
38	sankar	50	M	shopkeeper	P	P	P	P	A	A	P	A	P	103 F	138/90	P	P	P	A	P	P
39	adithya	32	M	teacher	P	P	P	A	P	P	A	A	A	102 F	144/86	A	A	A	A	P	A
40	naresh	36	M	coolie	P	P	P	A	A	A	P	P	A	101 F	90/54	P	P	P	P	P	P
41	indhumathi	38	F	house wife	P	P	P	A	A	P	P	P	A	101 F	156/96	P	A	P	P	P	A
42	manikandan	31	M	coolie	P	P	P	P	A	A	A	A	A	101 F	150/90	A	A	P	P	P	A
43	iyappan	78	M	farmer	P	P	P	A	A	P	A	A	A	100 F	92/68	A	A	A	A	P	A
44	george	69	M	teacher	P	P	P	A	A	P	P	A	A	102 F	124/82	P	A	P	A	P	P
45	atheeba khanam	17	F	house wife	P	P	P	P	A	A	A	A	A	102 F	90/54	A	P	P	A	A	A
46	murugan	22	M	coolie	P	P	A	A	A	P	A	A	A	100 F	176/94	A	A	P	A	P	A
47	eswar	25	M	farmer	P	P	P	P	A	A	P	P	A	102 F	138/90	P	A	P	P	P	P
48	ameena nahid	19	F	house wife	P	A	P	A	A	P	P	A	A	102 F	88/60	P	A	P	A	P	A
49	ramachandran	54	M	shopkeeper	P	P	P	A	A	P	A	P	A	101 F	142/98	A	P	P	P	P	A
50	sudheer	60	M	coolie	P	P	P	P	A	P	P	P	A	102 F	156/96	P	A	A	P	P	P

51	anthonysaamy	62	M	farmer	P	P	P	A	P	P	A	A	A	101 F	150/90	A	A	P	P	P	A
52	ganesan	58	M	coolie	P	P	P	A	A	A	P	P	A	102 F	142/90	P	P	P	P	P	P
53	dinesh	16	M	coolie	P	P	P	P	A	A	A	P	A	101 F	86/50	A	A	P	P	A	A
54	siva	21	M	coolie	P	P	A	A	A	P	A	A	A	102 F	120/80	A	A	A	P	P	A
55	meenakshi	23	F	house wife	P	P	P	A	A	P	P	P	P	104 F	118/90	P	P	P	P	P	P
56	sundar	22	M	coolie	P	P	P	P	A	P	A	A	A	102 F	138/90	A	A	P	A	A	P
57	joseph	64	M	shopkeeper	P	P	P	A	A	P	A	A	A	103 F	90/48	A	P	P	P	P	A
58	krishnan	52	M	teacher	P	P	P	A	A	P	P	A	A	102 F	142/98	P	A	A	A	P	P
59	anil	54	M	coolie	P	P	P	P	A	P	A	P	A	104 F	156/96	A	A	P	P	P	A
60	srinivasan	19	M	teacher	P	P	A	A	A	A	P	A	A	102 F	150/90	P	A	A	P	P	P
61	pichaisundaram	82	M	farmer	P	P	P	A	A	A	P	A	A	100 F	92/50	P	A	P	A	P	A
62	sathyaseelan	56	M	farmer	P	P	P	P	A	P	P	P	A	102 F	124/82	P	P	A	P	P	P
63	natarajan	64	M	coolie	P	P	P	A	A	P	P	P	A	101 F	120/80	P	A	P	A	P	A
64	shivasankar	53	M	farmer	P	P	P	P	A	P	A	P	A	102 F	118/90	A	A	P	P	P	A
65	ravi	20	M	coolie	P	P	A	A	A	A	A	A	A	103 F	122/86	A	P	P	A	P	A
66	ranjan	21	M	farmer	P	P	P	A	A	P	A	P	A	102 F	132/ 80	A	P	P	P	P	A

67	ibrahim	51	M	shopkeeper	P	A	P	P	A	P	P	A	A	101 F	124/60	P	P	P	A	P	P

35	19800	1.1	98	6	7.6	4.2	430	452	G	G	NG	NG	ARF, HP	13	discharged
36	9700	0.98	35	0.5	1	0.3	40	32	G	G	NG	NG	NC	5	discharged
37	16600	0.67	93	3.9	6.9	3.4	560	531	G	G	NG	NG	ARF, HP	11	discharged
38	4200	0.15	25	0.7	8.2	5.6	675	679	G	G	G	G	HP	9	discharged
39	17600	1.04	29	1	0.8	0.1	48	50	G	G	NG	NG	ARDS	10	discharged
40	4400	0.87	96	4.2	8.3	4.2	546	456	G	G	NG	NG	ARF, HP	14	discharged
41	19100	0.76	89	4.8	7.4	3.8	657	640	G	G	NG	NG	ARF, HP	12	discharged
42	21300	2.05	31	1	1.3	0.5	38	40	G	G	NG	NG	NC	5	discharged
43	3800	1.24	33	0.9	1.2	0.2	32	30	G	G	NG	NG	NC	5	discharged
44	16500	0.57	102	5.9	7.9	4.1	630	675	G	G	G	NG	ARF, HP	10	discharged
45	10000	0.98	30	0.9	1	0.1	30	40	G	G	NG	NG	NC	4	discharged
46	16500	0.95	28	0.7	1.1	0.2	49	44	G	G	NG	NG	MC	8	discharged
47	4500	1.43	73	7.2	9.7	5.7	658	675	G	G	G	NG	ARF, HP	9	discharged
48	15800	0.59	22	0.6	8.6	4.6	734	740	G	G	NG	NG	HP	7	discharged
49	15900	0.23	72	7.1	1.4	0.2	48	51	G	G	NG	G	ARF	8	discharged
50	16000	0.87	90	5.2	7.9	4.5	654	543	G	G	NG	NG	ARF, HP	10	discharged
51	17900	0.85	21	0.7	1.5	0.6	34	38	G	G	NG	NG	NC	5	discharged
52	10400	0.59	76	4.9	8.5	4.2	768	657	G	G	NG	NG	ARF, HP	10	discharged
53	11000	0.51	298	11.2	1.4	0.2	40	42	G	G	G	NG	ARF	9	died
54	9000	0.62	20	0.7	1	0.1	38	34	NG	G	NG	NG	NC	5	discharged
55	18500	0.18	101	7.9	7.8	3.5	546	576	G	G	NG	G	ARF, HP	10	discharged

56	6500	0.93	24	0.6	1	0.1	32	35	G	G	NG	NG	NC	4	discharged
57	18700	0.81	27	0.7	1.9	0.2	40	32	G	G	NG	NG	NC	5	discharged
58	5900	0.22	109	8.3	9.1	6.7	456	435	G	G	NG	G	ARF, HP	11	discharged
59	19700	0.91	87	5.4	1.3	0.4	39	40	G	G	NG	NG	ARF	9	discharged
60	6600	0.82	78	5.2	9	5.6	467	478	G	G	NG	NG	ARF, HP	10	discharged
61	9800	0.81	28	0.8	7.5	4.2	464	498	G	G	NG	NG	HP	7	discharged
62	19600	0.73	74	3.9	6.9	3.7	376	346	G	G	NG	NG	ARF, HP	10	discharged
63	8700	0.62	82	4.7	8.6	4.1	786	765	G	G	NG	NG	ARF, HP	13	discharged
64	6700	0.54	22	0.9	0.9	0.3	34	40	G	G	NG	NG	NC	5	discharged
65	9800	0.55	20	0.9	1	0.4	43	42	G	G	NG	NG	NC	5	discharged
66	14300	0.83	94	3.7	1.4	0.3	43	40	G	G	NG	NG	ARF	8	discharged
67	11500	0.93	44	1.4	7.6	3	564	456	G	G	NG	NG	HP	8	discharged

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID No.09/01/2015 Dt. 20. 01.2015
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "Clinical Profile of leptospirosis with special reference to multiorgan involvement in KMC". -For Project Work-submitted by Dr. Ibrahim Sameem Kan, PG in General Medicine, KMC, Chennai- 10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

20/1/15

GOVT. KILPAUK MEDICAL COLLEGE
20 JAN 2015
Kilpauk, Chennai-10.

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

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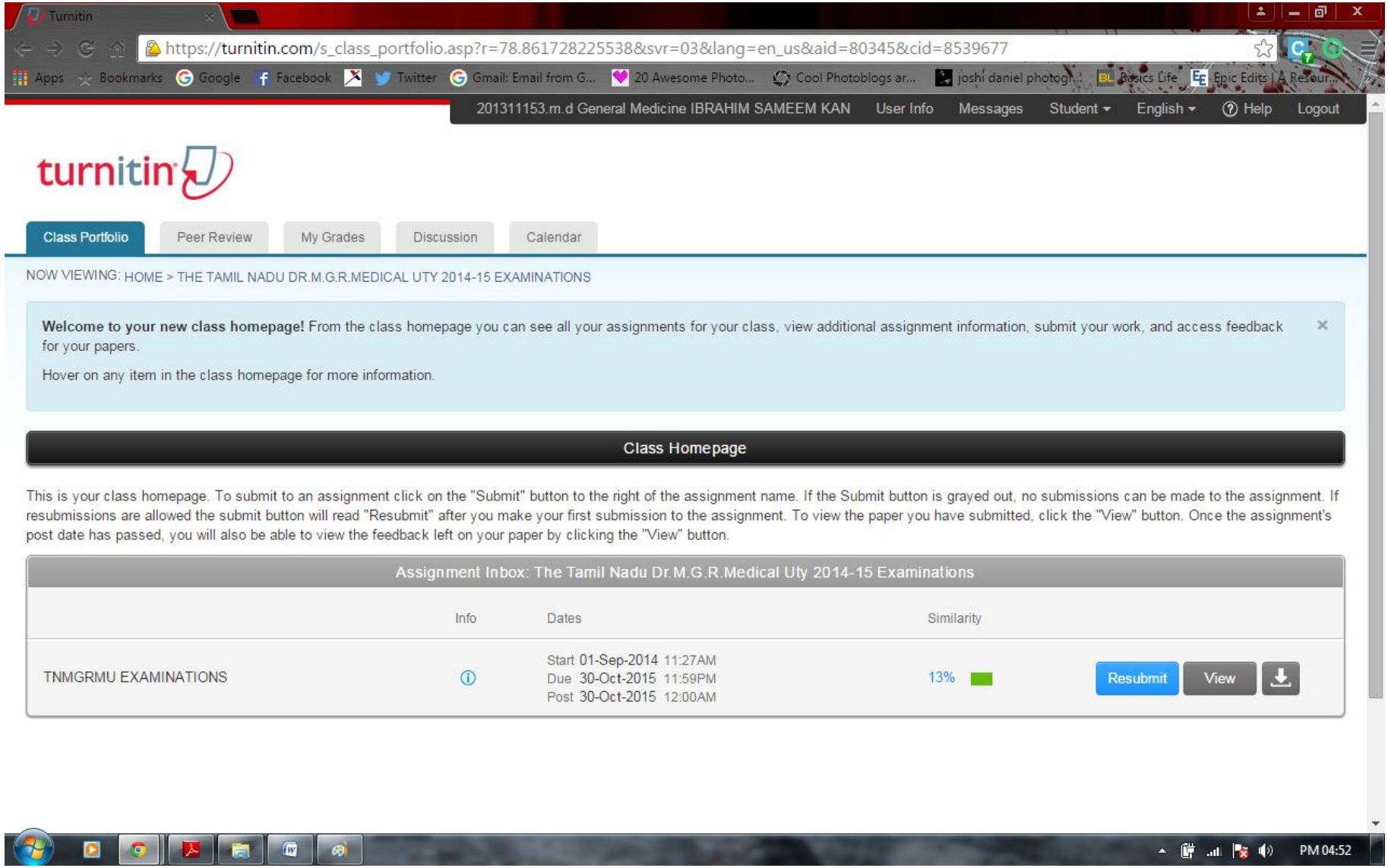
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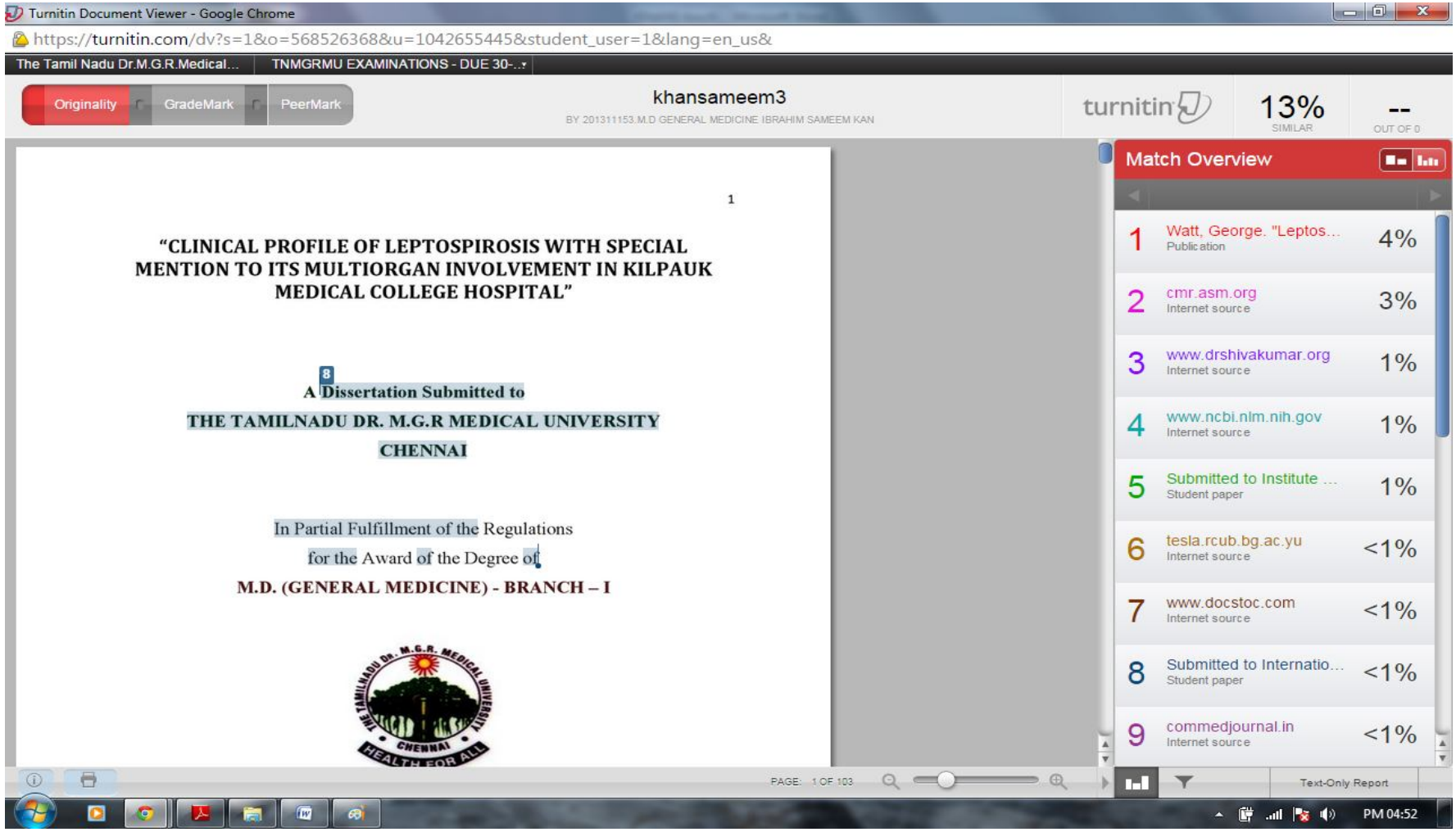
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A Dissertation Submitted to
THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY
CHENNAI
In Partial Fulfillment of the Regulations
for the Award of the Degree of
M.D. (GENERAL MEDICINE) - BRANCH – I
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